A

MANUAL

OF

GENERAL PATHOLOGY.

FOR THE USE OF

STUDENTS AND PRACTITIONERS OF MEDICINE.

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TRANSLATED FROM THE SIXTH GERMAN EDITION

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EDITOR'S PREFACE.

AFTER perusing the fifth edition of Wagner's Pathology in 1872 I was strongly impressed with the idea that it was well worthy of reproduction in this country. No book in the English language gives such a thorough *résumé* of the elements of medicine, and in none is the matter so arranged as to be available for both the student and the practitioner. This, the sixth German edition, is much improved, many references to publications in 1872 having been inserted; in many chapters the work is fully up to date. This elaboration is perhaps most evident in the sections on the theories of fever; where knowledge which could only be obtained by laborious work in a large city library is condensed within the compass of a few pages.

I have permitted myself to make very few changes from the original; two or three pages from the sections on soil and climate, and some short paragraphs in the chapter on fever, have been omitted. A few foot-notes and bibliographical references (chiefly American), and an index of authors, have been added.

My friend Dr. Van Duyn has translated at least two-thirds of the book. The proof-reading and arrangement of the work have fallen to my share. In our translation we have encountered some difficulties, and those who have done the same kind of work will know how to make allowance for a number of awkward sentences in the English. We have endeavored to be literal and at the same time clear; and elegance of style has not been aimed at.

The metric measures and the centigrade thermometric scale have been retained. I have done this in order to aid in diffusing knowledge of these now national standards, and to do a trifle toward bringing medical observers in this country into closer communion with the general scientific body.

E. C. SEGUIN.

NEW YORK, *January*, 1876.

PREFACE TO THE FIRST GERMAN EDITION.

THE authors of this work were closely united for nine years by common scientific interest and most intimate friendship, until the death of UHLE, in 1861, severed the relationship. As long as both of us labored at the same University, and in the same city, questions closely connected with general pathology formed the subject-matter of almost daily converse ; and hence the wish was often expressed that we should together write a manual on this subject. The execution of this plan was provisionally thwarted by the calling of one of us to a distant University.

For the possibility of fulfilling this long-postponed design, I am indebted to UHLE's widow, who bequeathed all his manuscripts to me. Upon perusing them I discovered that UHLE had carefully elaborated just those chapters which had been only incompletely filled in my work. This book is the product of the union of both manuscripts.

As regards the division of labor, it should be stated that the first part in plan and for the greater part in execution is by me ; the second part, with the exception of the last chapter, by UHLE ; the third part is mine, with the exception of some passages in various chapters, and of the article " Fever," which was planned by UHLE.

Thus much in regard to the origin of the book. As regards the conception of the whole, the grounds upon which this conception was based, and all other points, the work must speak for itself.

E. WAGNER.

LEIPZIG, *March*, 1862.

PREFACE TO THE SIXTH GERMAN EDITION.

THE present edition has been augmented in every part. It has thus become more voluminous than I might have wished; but I hope that the utility of the book has not been injured by this, because I have as much as possible endeavored to thoroughly sift important facts on the one hand, and on the other to present in smaller type documentary evidence and matters of less importance.

The preparation of this edition has been more difficult than that of the others, chiefly because of three evils with which our literature is afflicted. These are: in the first place, the preliminary communications which usually are not followed by confirmatory statements; second, the large number of publications about experiments which are occasionally useless; and, third, the present condition of the question of fungic diseases.

For the account of Fever, and for several sections on ætiology (Ground, Climate, Dwelling), I am indebted to Prof. THOMAS. I also wish to express my thanks to Prof. HUPPERT (5th Ed.), and to Prof. F. HOFMANN (6th Ed.), for many chemical explanations.

E. WAGNER.

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PART FIRST.

GENERAL NOSOLOGY.

GENERAL CONCEPTION AND FORMS OF MORBID STATES.

PATHOLOGY is the knowledge of disease; GENERAL PATHOLOGY is the knowledge of the morbid state and of disease in general; SPECIAL PATHOLOGY is the knowledge of individual diseases.

It is impossible to give a short and clear definition of disease. Usually disease is referred to as the condition opposed to health. Both expressions are in common use.

That individual is healthy, in whom the more important phenomena of life (nutrition in its widest sense, development, and reproduction; movement, sensation, and psychical activity) take place quietly and uniformly, and who has the sense of well-being. If we attempt to make the conception of health more clearly defined, it is easy to fall into absurdities. For, in a scientific conception of health, it is necessary to suppose that not only all parts of the body perform their normal functions, but also that they are normally associated. And yet in this there may occur great deviations from the ideal type, and the affected person remain well and live long. In a strict scientific sense, it may be said that no one is healthy.

He is sick in the sense above referred to, in whom the phenomena of life are disturbed, or upon whom external physical and chemical agencies act with unwonted energy. In consequence, the affected person usually has a feeling of ill-health. Yet this conception of sickness is too limited; since a person may for a time appear to exhibit normally performed functions, and may have the feeling of complete health, and yet be seriously ill.

Consequently, in the conception of disease, we must include not merely modifications in the state of feeling and in the performance of function, but also the more considerable alterations of the normal structure, and composition of single or numerous organs.

It follows that health and sickness are only relative and conventional conceptions; that the healthy state very gradually passes by many intermediate conditions into the decidedly sick state; that health and disease are not absolute opposites.

Sufficient synonyms of the word disease are the expressions complaint, affection, disorder. Others are occasionally made use of, as, for example, abnormality, which are not exact equivalents, because while the conception of the normal is ideally well defined and invariable, that of health is broad, and an individual may be said to be perfectly healthy in spite of the presence of various abnormalities (scars, defective external parts, absence of one kidney, etc.); the abnormalities only becoming diseases when they inter-

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fere with important functions, produce pain, etc. Lastly, several expressions are in use to convey the notion of slight sickness, as, for example, indisposition; and to express such conditions as arise in consequence of disease, but which are partially cured, or which can have no influence upon the general organism. The words malformation, deformity, are applied to such as occur in fœtal life, and defect, *vitium* (for example, amputation-stumps, mutilations, warts, etc.), to those arising after birth.

The so-called feeble health (bodily weakness, valetudinary state) is easily changed into disease by the action of slight causes. It is congenital or acquired. It is often met with in the convalescence from severe diseases. It is not rarely simulated by a progressive disease which cannot be diagnosed in that early period; as, for example, phthisis.

The disturbances which constitute disease are ANATOMICO-PATHOLOGICAL (that is to say, histological), or, CHEMICO-PATHOLOGICAL, or functional.

ANATOMICO-PATHOLOGICAL and histologico-pathological, or morphological alterations (defects of form) are all those in which the physical relations of the part are changed. These changes consist sometimes in general swelling (inflammation of the subcutaneous connective tissue), sometimes in alterations of consistence (thickening of the skin, softening of the brain), sometimes in the filling or coating of surfaces, previously exposed to the air, with dense material (laryngeal croup, inflammation of the lungs), sometimes in disturbance of relations (wounds), sometimes in microscopical changes in the cell-contents (fatty change, etc.).

CHEMICO-PATHOLOGICAL disorders (defects of composition) are either such as manifest themselves by altered quantity of a chemical ingredient of the body, as variable amounts of blood constituents, urinary substances, etc., or by altered quality of the same, as, for example, change in the fibrin after frequent venesections; or such as consist in the existence of an ingredient in an abnormal situation, or in abnormal quantities, as albumen or sugar in the urine, urea or bile in the blood, uric acid in joints.

Alterations of form and composition always appear together. This follows from the processes of growth and nutrition in the healthy state, in which the formation of a single cell without chemical activity is unimaginable. And we also have a proof of this in the direct observation of the majority of those diseases which have been studied histologically and chemically.

FUNCTIONAL or SYMPTOMATIC (or dynamical) disorders are those in which we have, as yet, been unable to detect any material lesion. This, for example, is often the case in pain and convulsions. And yet in these conditions we must admit the existence of delicate material alterations, which are not recognizable with our present means of investigation.

In many cases it is furthermore important to recognize an affection as IDIOPATHIC or SYMPTOMATIC: it is called symptomatic if another cause is present to account for the general phenomena, especially fever, as for example, roseola in typhoid fever, *herpes labialis* in intermittent fever, pneumonia, etc.; contrarily, when no other cause for the general symptoms, particularly fever, can be made out, the affection is called idiopathic, as roseola æstiva, autumnalis, herpes of the lip, etc.

Every alteration has a defined seat. The causes of disease do not usually affect the whole body, but only a portion of it; at times a tissue, an organ, or a part of an organ, at times a system of tissues or organs. In the affected part there must next ensue a specified change in substance, an anatomical or a chemical alteration, or both together; so that we may maintain that, at least in the beginning, every alteration is local. It is

possible that the *post mortem* examination of the organs and tissues does not enable us to determine this localization with certainty ; anatomical investigation is not the only means of contributing knowledge to pathology.

LOCAL DISEASES are restricted to a tissue, an organ, or a portion of one, during their whole existence (local diseases, local affections) ; or they may extend, or become generalized.

EXTENSION OF DISEASE takes place in three principal ways : 1st, by continuity and by contiguity ; 2d, by way of the blood and the lymph ; 3d, through similarity in the structure and functions of tissues and organs.

THE EXTENSION OF DISEASE BY CONTINUITY AND CONTIGUITY is easily demonstrable by sufficient anatomical knowledge. We see, for instance, a spreading by continuity in the catarrhal inflammation of the nasal mucous membrane, which may extend to the frontal sinuses, to the antrum of Highmore, sometimes to the lachrymal ducts and conjunctivæ, or to the Eustachian tubes and the middle ear, to the cheeks and pharynx, sometimes to the larynx, trachea, and bronchial tubes. An extension by contiguity we meet with in many affections of the serous membranes ; a progressing inflammation of the stomach or intestinal canal frequently produces inflammation of the contiguous part of the parietal or hepatic serous membrane. The extension of disease by continuity and by contiguity together, we see best illustrated in the serous membranes. A superficial gangrene focus in the lung tissue will, for instance, cause a consecutive inflammation of the pulmonary pleura just over it, and this, in its turn, will extend by continuity over the remainder of the pulmonary pleura, and by contiguity to the costal or diaphragmatic pleura.

Upon serous membranes the spreading of inflammation takes place in different ways, according to the seat of the primary inflammatory focus. In the neighborhood of the apex and the posterior aspect of the lung, at the place of origin of the great vessels from the heart, at the relatively immovable segment of the stomach (the smaller curvature) and the intestinal canal (cæcum), the inflammation more easily remains circumscribed, while in other much more movable parts of the membranes it extends easily throughout the latter. In young individuals diseases of the epiphyses seldom extend to the diaphyses ; which is accounted for by the fact that the epiphyses and diaphyses have each their proper blood-vessels, which, for the most part, do not communicate with each other. In this connection we might mention many inexplicable phenomena. Whereas, for example, cancer of the cardiac orifice always implicates, sooner or later, the stomach and œsophagus, cancer of the pylorus seldom attacks the duodenum.

The extension of disease by continuity and by contiguity must be understood to be such in a macroscopic sense. To the microscope the relation of parts is very variable in different tissues ; sometimes the cells lie thickly one upon another (epithelia cells), or they may be separated from one another by interstitial substance, or connected by means of processes (corpuscles of connective tissue, bone-corpuscles, ganglion-cells), or they may be wholly isolated in a fundamental tissue (cartilage-cells).

THE EXTENSION OF DISEASE THROUGH THE BLOOD AND LYMPH occurs in one of three ways. The substances contained in the vessels are carried forward by the current of blood or lymph, and deposited in other parts of the vascular system (coagula, bits of valves, etc.) ; or, substances originating outside of these vessels enter them (bile, urea, uric acid, lime-salts, fat, etc.) ; or, lastly, when substances from without the body enter the vascular system (dust, parasites, poisons).

THE SPREADING OF DISEASE IN SIMILAR TISSUES OR SIMILAR ORGANS does not at the present time admit of any satisfactory explanation, unless the histological and physiological identity of the blood and the nerves, as well as the causal influences, be taken into consideration. As examples of

this sort of extension, we may cite affections of the connective tissue of external and internal parts (inflammation); of the bones (inflammation, tuberculosis); of the joints (articular rheumatism); of the serous membranes (inflammation, tuberculosis, cancer); of the skin (many forms of erythema, erysipelas, eczema, psoriasis, syphilides, etc.), and diseases of double organs, especially the eyes and kidneys.

Whereas, most double organs are symmetrically diseased, or at least certain diseases manifest themselves symmetrically (tuberculosis of the lungs, syphilis of the testes, inflammation of the kidney, and the kidney affections known by the name of Bright's disease, etc.), there are many diseases which appear only in one of the double organs (as, for example, primary cancer of the eyeball, of the lung, of the kidney, testis).   This is also in part true of both sides of the heart, the brain, the thyroid gland, etc.

As regards the extension of disease through the medium of the nerves, that is to say, in a reflex way, our knowledge is as yet so imperfect that we have no wish to enlarge upon it here.   That this does take place in the above-named way, by reflexion from sensorial, sensitive, and motor nerves upon sympathetic nerves, has been rendered certain by researches upon the sympathetic.

The so-called sympathetic affections of the eyes are of great practical interest in this respect (VON GRÆFE, MOOREN, and others. Consult PEPPMÜLLER, *Arch. v. Heilk.*, 1871, xii., p. 219; *POOLEY, N. Y. Medical Journal*, Oct. 1870).

GENERAL OR CONSTITUTIONAL DISEASES affect either the entire organism, or several different organs, or tissue-masses. Those general diseases in which altered composition of the blood is demonstrable are called dyscrasiæ, blood-diseases (for example, chlorosis, icterus, anæmia); those which become general through the medium of the blood, when the blood has probably taken up some poison, without an evident change in the composition of this fluid, we name intoxications, or infectious, toxic diseases; Intoxication, when the injurious substance is derived from the inorganic or vegetable kingdoms (*e.g.*, lead poisoning, opium intoxication, probably malarial disorders); Infection, if the poison is received from a diseased animal (*e.g.*, glanders, anthrax, hydrophobia), or from a diseased human being (*e.g.*, measles, small-pox, hiccough, typhoid fever, cholera, syphilis).

EVEN IN THE CASE OF GENERAL OR CONSTITUTIONAL DISEASES, THE LESIONS USUALLY INVOLVE ISOLATED ELEMENTS.   If very many local disorders exist, the disease appears to be general because of its numerous foci.   VIRCHOW has particularly called attention to the existence of such local morbid conditions in general diseases, even in their latent stages (as in syphilis).

The expression localization of disease implies that the morbid state is at first general and afterward becomes local.   The knowledge of the local importance of every disorder contradicts this assumption.   And yet, the doctrine of the localization of some general diseases in certain stages is sometimes correct.   In nearly all intoxications the poison, be it lead, measles, or typhoid-fever poison, first makes a local impression; it enters the blood through the digestive or respiratory organs, after which there elapses a certain period of time, during which it is impossible to say in what part of the body the subsequent morbid lesions will appear.   When these last are perceptible, it is said that the disease has localized itself here and there.   The expression has likewise been employed to designate diseases which have always been recognized as local; as, for example, inflammation of the lungs.   In this disease there often pass by one or two, or even three or five days, in which the symptoms of a severe illness are recognized, but in which there are no signs pointing to the lungs as the seat of the affection.   If it be said that the disease has localized itself in the lungs, we only mean that the local starting-point of the disorder could not sooner be recognized.

There are still other modes of conception of disease which have been made use of to designate tendencies in medicine.

Just as pathologists at various times have considered the humors or the solid parts of the body as the starting-points and channels of propagation of disease, so phy-

sicians have distinguished themselves as HUMORALISTS or SOLIDISTS. Among solidists the NEURO-PATHOLOGISTS and CELLULAR PATHOLOGISTS must be separately designated. It is the aim of cellular pathology to place our anatomical notions of disease upon an histological foundation, *i. e.*, to connect them with the smallest integral parts which the microscope can discover. It is important enough that our general notions should be sensorial in so far as is possible; but it was an error to suppose that cellular pathology embraced the whole of pathology. For the latter the blood and nerves are quite as important as the cells of organs.

In earlier times disease was looked upon as something foreign to the organism, as something forced upon it, as something separate from the life of the body. This conception, according to which disease was a particular entity (*on, ens.*) which lodged in the body, was called ontological. Many went so far as to speak of disease as embodied. Many expressions still in common use, as " the disease attacks the body," " the body struggles with the disease," " the physician combats the disease," " nature has overcome the disease," etc., serve to remind us of the older notions.

Again, medical men have been designated as EMPIRICISTS and RATIONALISTS in matters of pathology, but more in regard to therapeutics. He is an empiricist who reasons as little as possible, does not concern himself about the explanations of separate symptoms, or of the mode of action of medicaments, but who relies on experience. If he be old in years, and ripe in so-called practical experience, he will attach especial importance to his own observations. On the contrary, those physicians are called rationalists who do not value the facts themselves so highly as their explanation, and who seek the advance of pathology in the connecting of every morbid manifestatation immediately with physiological data. From this, however, nothing can issue but a pathology whose facts are taken from the sick, together with certain associated physiological hypotheses.

Lastly, much is said of ANATOMICAL and PHYSIOLOGICAL medicine. The anatomical school busies itself with the investigation of anatomical changes in the diseased organs and their relation with the symptoms exhibited during life. All important progress in medicine has been dependent upon anatomico-pathological discoveries. Up to the present time no method of study has penetrated so far towards the seat and causes of disease as pathological anatomy. The anatomical study of disease, as well as its histological or cellular study, is provisionally the most solid basis for our reasoning. And yet pathological anatomy cannot by itself explain the relations of phenomena in the sick; this is best done by a knowledge of similar processes in the healthy body, and the study of morbid processes by all the methods which are used in physiology for the investigation of the functions of the normal body. This is physiological medicine.

The correctness and importance of the pretension to build up pathology upon a physiological basis rest upon these two considerations. First, it is necessary to maintain the elementary notion that morbid processes do not essentially differ from normal ones: each morbid manifestation finds its analogue, in physiological conditions and processes. There are no specific chemico-pathological bodies. Leucin and tyrosin, which were looked upon by their discoverer as the cause of the nervous symptoms in atrophy of the liver, were soon proven to be usual constituents of the healthy body. There are no specific pathological forms. It was believed, a while ago, that peculiarly formed cells could be said to exist in tubercle, sarcoma, cancer; a statement which has been shown to be false. There are no specific pathological symptoms; even the venous pulse, which is only met with in morbid states, has its analogue in the arterial pulse.

We may, as has been done by VIRCHOW, designate the general morbid processes as HETEROCHRONIC and HETEROTOPIC : that is to say, as processes which would be called normal, did they take place at a different time or in a different spot. For example, an effusion of blood in the ovary at the time of menstruation is normal; an effusion of blood into the brain is always abnormal, and is the cause of other morbid phenomena ; we have here HETEROTOPIA. Hemorrhage from the mucous membrane of the uterus at a certain time (menstruation) is normal; at other times abnormal, HETEROCHRONIA.

There is no radical difference between the forces and the substances by means of which normal and morbid life is kept up; no important difference between physiological and pathological laws. The difference lies in the conditions under which the forces and substances of the body operate.

The second important factor which is fundamental in the conception of physiological medicine, is the manner in which the altered, that is to say, pathological phenomena of life are investigated. This is the so-highly praised physiological method. However, physiology knows no methods save those of chemistry, and chemistry none

save those of physics. Surely a knowledge of diseased life presupposes a knowledge of healthy life ; pathology assumes the existence of physiology. Pathological phenomena must be studied by themselves, and though one may be a very good physiologist, and not understand all the phenomena of the sick-bed, yet we may speak of a pathology built up by scientific methods ; although in the strict sense of the word, a special physiological medicine is an empty phrase.

THE SOURCES OF GENERAL PATHOLOGY as well as those of practical medicine, are PHYSICS, CHEMISTRY, ANATOMY, and PHYSIOLOGY. To be more particular, there are four branches from which the materials of general pathology are chiefly derived : OBSERVATION AT THE BEDSIDE, EXPERIMENTATION, PATHOLOGICAL ANATOMY, and PATHOLOGICAL CHEMISTRY.

OBSERVATION AT THE BEDSIDE, which includes the special pathology of internal and external diseases, as well as all those associated branches which have in later years been separated from it, such as pathological chemistry and physics, stands in the most intimate relation to general pathology ; every progress in the former naturally benefits the latter, and *vice versa*.

EXPERIMENTAL PATHOLOGY presents the same advantages, and is open to the same objections as experimental physiology. The real value of the experiment consists in that it can be performed under determined circumstances of place, time, and conditions ; the latter may be indefinitely varied, and death can be induced at a precise period after the experiment. These advantages are offset by a variety of serious disadvantages. A number of deeply placed organs are not at all accessible, or only made so by the injuring of other almost equally important parts ; most experiments are accompanied by disturbing complications (hæmorrhage, pain, agitation;) experimental assaults are usually much more violent and more sudden than are lesions of so-called spontaneous origin ; weak, or gradually encroaching irritation is not feasible in many parts. Furthermore, the experimenter has to contend with peculiar difficulties in individual organs or systems ; in the nervous system, for example, no conclusive experiments can be made upon the higher senses, or upon the higher psychical functions ; and farther, experiment is useful only for perceiving the occurrence of strongly marked symptoms, for slight irritations or palsies usually escape observation ; and, lastly, there is a whole series of lesions which appear in man and in animals spontaneously, or from the operation of unknown causes, and which cannot be reproduced by experiment, such as for example, as the atrophy of amyloid degeneration, cancer among new-formations, etc.

In spite of these drawbacks we owe to experimentation a series of the most certain and beautiful observations of general pathological interest. We will mention only a few, such as have benefited pathology relatively more than physiology. In the first place, there are a number of questions in ætiology to which experimentation has given exact answers. This has been the case with regard to the origin of most of the so-called mechanical and chemical, or toxic diseases, with regard to the transfer of several vegetable and animal parasites, particularly tænia and trichina, with reference to vaccination most notably, and with regard to the inoculability of syphilis and tubercles. That ætiology will be a true one which shall be based upon conclusions derived from experimental pathology, and shall not, as at present, consist in great part of a fruitless chaos of real and imaginary causes of disease. But to this end a preparatory schooling is necessary, which few experimenters possess, including a theoretical and practical knowledge of physics, chemistry, physiology, and pathology, as well as the spirit not to shrink from making difficult preliminary studies before undertaking the solution of seemingly simple questions.

There are also some processes for a complete explanation of which pathology is indebted in part to experiment, and in part to observation at the bedside. We will recall only the observations upon the regeneration and new formation of tissues, in particular the connective, bony, and muscular tissues, the blood-vessels, and nerves; to the alterations in the blood during stagnation of the fluid within the vessels, or in extravasations; to the appearance of hyperæmia after section of the sympathetic; to the various inflammation experiments, the old observations upon the transparent parts of animals, and the recent ones by section of certain nerves; to the experiments upon the derivation of pus; to the experiments upon thrombosis, embolism, and the long series of observations upon pyæmia; to experiments demonstrating the mechanical production of many dropsies; to experiments upon the origin of fever, icterus, uræmia, diabetes, tuberculosis, etc.

PATHOLOGICAL ANATOMY has exerted an extraordinary influence upon general pathology in two ways; by the reformation of medicine in general, as well as by the discovery of a mass of peculiar histologico-pathological facts.

The first point, the overthrow of the ancient symptomatic medicine by pathological anatomy, is, in general, well understood. "The progress of medical science has been from the first intimately bound up with the progress of anatomy." "Pathological anatomy must be considered as not merely the foundation of medical knowledge, but also of the medical art, since it contains all that is positive knowledge in medicine, or the foundation of it." Pathological anatomy has newly discovered a great number of diseases, which have symptoms apparently just like those of other diseases. This science has made it possible that our so-called physical diagnosis should have reached so high a degree of perfection as it has. Such affections as are not demonstrable by means of the scalpel and microscope are, with very few exceptions, exceedingly obscure.

The influence of pathological anatomy and histology upon general pathology became more specially secured by means of the microscope, to which alone we are indebted for a wholly new science, the general anatomy of the healthy and diseased tissues of the body. This influence is most apparent in the knowledge of the causes and consequences of hæmorrhage, thrombosis and embolism, gangrene, dropsy; in the knowledge of inflammation; in that of atrophies and new-formations.

PATHOLOGICAL CHEMISTRY has not merely contributed to our knowledge of numerous special diseases (renal affections, etc.), and of general pathological processes (fatty and pigmentary degenerations, many so-called diseases of nutrition), but it also first enabled us to know well the nature of several diseases, such as diabetes mellitus, uræmia, general fatty degeneration, etc.; and it has thus become one of the important supports of general pathology. All great advances in the next few years must be looked for in this line of investigation.

These are the sources whence has come our knowledge of general pathology, and it is from them that its future development is to be derived. Bedside observation should be as painstaking as possible, and each individual case should be investigated by the help of all means of examination. It is only too true that such complete analysis is possible only in well-organized hospitals. On the other hand, it should be borne in mind that a host of questions are to be solved only in private practice, and by the family physician. Unfortunately the latter now withdraws from the proper cultivation of science, and would hold the hospital physician responsible for future progress. Experimentation should fulfill the conditions pointed out

above, and be brought into use only where exact investigation of the patient and *post mortem* examinations fail to yield the solution. Lastly, pathological anatomy should perform a double function; it should on the one hand, and that perfectly independently of medical observation, endeavor to define all alterations of the organism, with full histological and histo-chemical details, more especially, however, in their genetic relations, and their behavior toward the organization in general. On the other hand, it should be closely united with clinical observation, and should study after death the alterations recognized in well-observed cases during life. Lastly, pathological chemistry should, in conjunction with the above means, particularly bedside observation, become our most important aid.

At different epochs some of the above-named sources of knowledge have been especially cultivated. In the last few years this has been true of experimental pathology, which has been employed by a few experts and by many inexperienced men, and which has injuriously been brought in to complicate clinical questions, causing errors which cannot be avoided by the use of that method alone.

GENERAL SYMPTOMATOLOGY AND DIAGNOSIS.

The phenomena of disease, those alterations in the physical, chemical, and vital attributes of the body which are noticeable by the physician and the patient, are called, in distinction from the phenomena of healthy life, SYMPTOMS or SIGNS of disease. The knowledge of these signs constitutes SEMEIOLOGY or SYMPTOMATOLOGY. The art not merely of concluding from them to existing local alterations, but also of obtaining a knowledge of the compatible and actually existing conditions, or, as is said, the art of making a diagnosis, is called DIAGNOSIS.

In earlier times it was more usual to make a SYMPTOMATIC DIAGNOSIS; we were contented with the determination of the most striking symptoms, and we consequently spoke of fever, pain, spasm, dropsy, jaundice, without taking into consideration the causes of these conditions. Even at the present day we must often remain contented with such a statement. It is possible, however, in many cases to ascertain the existence of definite alterations upon which the phenomena depend; this constitutes the ANATOMICAL DIAGNOSIS.

The requirements of a complete diagnosis include not merely the recognition of the organ chiefly diseased, but also that we should obtain as thorough a knowledge as possible of the condition of all the organs, by an examination of the patient by all the means in our power.

There are a few symptoms whose presence indicates with certainty, and even necessity, the existence of certain conditions—the so-called PATHOGNOMONIC SYMPTOMS; such as the pulsation of the jugular vein at the base of the neck, and the hepatic pulsation in insufficiency of the tricuspid valves, the rust-colored sputa in pneumonia. Such symptoms are however few, and their number has diminished more and more with the growth of pathological knowledge. Nearly always we cannot conclude from a single symptom to the existence of a given morbid state; we must consider a number of symptoms together.

The term NEGATIVELY PATHOGNOMONIC SYMPTOMS may be given to such as do not at all, or hardly ever occur in certain diseases—as *herpes labialis* in typhoid fever, many temperature changes in various diseases.

Symptoms are commonly divided into DIRECT and INDIRECT. The direct are such as depend immediately from the altered organ, such as, for example,

the color and other peculiarities of the skin, the volume of organs, their hardness or softness, unevenness or smoothness. Indirect symptoms are the consequences of certain states of organs, whose direct examination is not practicable. The pulse belongs to this class in that it sometimes indicates disease of the heart and arteries, or morbid states of other organs. Many alterations of the urine and sweat belong to the class of indirect symptoms, as in hepatic and cerebral diseases; some disorders of the stomach are indirect symptoms of renal disease, etc.

Besides, we separate functional from statical symptoms. Functional or active symptoms give information respecting the degree and mode of activity of organs, as movements, sensations; as, for example, dyspnœa, pain in the chest in thoracic diseases. Passive or statical symptoms indicate only certain localized conditions of organs, as changes in the form of the thorax, and alterations in the structure and texture of parts.

Furthermore, symptoms are designated persistent when they occur throughout a disease; and intercurrent when they show themselves from time to time.

Very important is the distinction between OBJECTIVE and SUBJECTIVE SYMPTOMS. By the term subjective symptoms, we understand such as the patient himself feels, as pain, a sense of pressure, of constriction, etc. They are modified in the most varied way by the peculiarities of patients. They are more prominent in young and pampered individuals, whereas many severe diseases in old age are distinguished by the absence of these signs. In this class, the first rank is occupied by the symptom of pain, *i.e.*, abnormal irritation, or abnormally increased activity of sensitive nerves.

Objective symptoms are such as the physician can observe and appreciate through his senses. To this end we use the eye, inspecting directly as in cases of disease of the skin and accessible mucous membranes; or with the help of illumination, as with the ophthalmoscope, laryngoscope, specula, etc. Sometimes we employ the ear, as in studying the phenomena of percussion and auscultation; at others the tact, in order to ascertain the changes in the consistency of parts, for the study of tumors, of pulse-changes, to examine the vagina, rectum, etc. To this category we must also add all the results obtained by measurement, weighing, by the thermometer, by microscopical and chemical examination, etc.

The value of various symptoms in the critical appreciation of a case is of course very different. In general the value of a sign depends upon the clearness and certainty with which it can be made out, and also upon the degree of certainty with which its production can be traced to a particular organ. In consequence of the greater degree of positiveness they bring with them, objective symptoms are of much greater value than the subjective.

Among objective signs there are some which are brought to light by physical, chemical, or microscopical methods of investigation, and which are peculiarly reliable and valuable. The most objective, and better named most PHYSICAL SYMPTOMS, are such as are not merely observed by means of instruments, but which are in themselves measures of the amount of the phenomena. To this class belongs thermometry; for, while the estimation of skin heat by the hand is in the highest degree fallacious, by the correct application of the thermometer we not only obtain the exact temperature as a fact, but we also thereby obtain a measure in degrees of the amount of fever present. On the other hand, it is a misuse of the term physical if we speak of auscultation and percussion as "physical diagnosis;" because much more depends upon the experience of the observer and the dexterity of his hands in percussion than upon accuracy of hearing; and we possess no

objective measure for the phenomena, such as, for example, clear and dull sounds.

In order correctly to appreciate phenomena, even the objective, we not only need a knowledge of anatomy and physiology, of pathological anatomy, pathology, etc., but also special preparation and experience. Above all, we must know what to look for, what to observe, and we must also be expert in those methods by which the phenomena are noted at the bedside. The physician of to-day must possess more than mere technical knowledge, he must have that skill which is only to be acquired by instruction and industrious practice (WUNDERLICH).

LATENT DISEASES are such as remain wholly or partially concealed from the physician in all or many cases, at their beginning or during their whole duration. This is either because the organs, with which they are connected, are inaccessible to examination (many parts of the lungs, the liver, pancreas, etc.), or because the functions of the parts are not known (certain brain regions), or because the disease is very much restricted (many pulmonary inflammations, cancer of internal organs), or because they are developed slowly and the physical properties and the functions of the organ are not perceptibly modified. Many diseases, serious in themselves, remain latent, because, as a consequence of their existence, compensatory conditions are developed, in consequence of which they (the diseases) remain without symptoms; for example, hypertrophy of muscular organs behind narrow places, as at the cardiac orifices, the digestive apparatus, the urethra, in collateral circulation, etc.

The subjective symptoms of severe disease of an organ not seldom remain latent, if another organ be equally or more severely affected; as, for instance, the symptoms of pulmonary tuberculosis in cases of extreme tuberculosis of the larynx or intestines.

Very often the phenomena lead us to suppose that there is disease of a part, without being sufficient to enable us to determine the nature of the disease.

The concealment of a disease is often only relative. For in the majority of cases the symptoms can only be discovered by peculiar methods of investigation and by modes of reasoning, it follows that their discovery will depend upon the individual degree of skill, knowledge, and the faculty of judgment of the investigator.

The further subdivision of symptoms into primary and secondary, essential and accidental, consensual or sympathetic, local and general, is in part self-evident and in part worthless.

There are three ways to arrive at a diagnostic judgment. These are of different degrees of value and certainty. If we wish to proceed safely we must not follow the first and second ways alone.

THE FIRST METHOD IS DIAGNOSIS AT A DISTANCE, THE RECOGNITION OF THE DISEASE AT A FIRST GLANCE. In many diseases of the skin, of the mouth, and pharynx, of the joints, a single inspection is sufficient. In other diseases, however, to content one's self with such an examination would prove most superficial, and would often lead into error. In this connection we should take note of the general impression made upon us by the patient; and this becomes more instructive for the physician the more he has the habit of quickly analyzing a patient's general appearance. Even if we cannot, in this manner, recognize the disease itself, we may often obtain information of use in determining the location, degree of severity, and danger of the disease. We use the same procedure in daily life. If we

meet a stranger, we conclude from physiognomy, the expression of his eyes, his gestures, his deportment, from the first impression we have of the development of certain parts of his body, to his inner psychical life, his character, his education, occupation, his ruling ideas and pursuits. In the same way the expert can, from the color of the face, from the facial expression, the posture, mode of lying, the walk of the patient, from his manner of breathing, of speaking, etc., often draw apposite conclusions as to the nature of the disease.

THE SECOND WAY TO FORM A DIAGNOSIS CONSTITUTES DIAGNOSIS FROM THE ANAMNESIS, that is, from the story which the patient tells of his illness. This account usually consists only of a recital of sensations of the most varied kind, intermingled with conjectures upon the origin of the disease. If the patient be competent to give a chronological account of the course of his ailment, it is sometimes possible to draw some conclusions from the often confused story as to the condition of the patient's body. It is necessary to understand popular expressions in order to be able to translate their vague import into medical language. The physician is sometimes obliged to give advice to and treat patients at a distance upon such sources of information transmitted by letter. It is well always to do this with the greatest caution, for it is natural that incomplete observation should lead our judgment into error.

THE THIRD AND SUREST DIAGNOSTIC PROCESS IS THE OBJECTIVE INVESTIGATION. We in this way seek to convince ourselves by actual sensorial observation of the anomalies presented by the diseased organism. In order to arrive at the most positive and comprehensive judgment of the condition, it is not sufficient to investigate that part of which the patient complains, but we must inquire into the state of every part of the body, and the condition of every function. This last rule is essential if one means to proceed in a well-grounded and certain manner. The physician's art consists mainly in the thoroughness of his examination. Without this, in spite of thorough scientific acquirements, he remains practically a useless man.

THE EXAMINATION OF PATIENTS consists of two parts.

The first is devoted to the obtaining of the ANAMNESIS (or HISTORY OF THE CASE). The conversation is most properly begun by a general inquiry, What do you complain of, where is your trouble? Then the patient may be allowed to talk uninterruptedly for awhile, but, as soon as he wanders off to irrelevant matters, as he commonly soon does, then it is necessary to ask special questions. In order to reach a conclusion in as short a time as possible, and to demonstrate our interest in the patient's condition, we first investigate the organ or function which he believes to be in a morbid state.

For example, if the patient complain of chest symptoms, we are to proceed at once in this direction. The important points in this connection are : Cough, how much, at what time of the day ; if chronic, whether it be actually present, or at times altogether wanting ;—Expectoration, its looseness, quantity, and color ;—Dyspnœa, whether when at rest, or excited by movement ; —Pain, dull or sharp ; its seat, whether in the centre or side of chest ; —the mode of lying, whether upon the right or left side, or if possible on both sides. And for the larynx, hoarseness, etc. ; for the nose, bleeding, etc.

In an analogous way the physician should investigate the condition of the digestive organs, the urinary apparatus, etc., and inquire into alterations of nutrition, into the presence or absence of fever.

If we wish to make a more special inquiry, it becomes necessary to ascertain exactly the duration and course of each individual symptom, and, espe-

cially in chronic diseases, to determine all the circumstances which have caused improvement, or which have made the disease worse.

Questions concerning the name, age, and condition of the patient, which usually in hospitals precede the examination of the patient, should in private practice be asked at the close of the examination, or casually during it. Inquiries into the causes of disease in general, into the health of parents, grand-parents, sisters and brothers, into the dwelling, victuals, clothing, habits (as, for example, indulgence in alcoholic drinks, in smoking, exercise, sexual intercourse, into previous diseases, especially syphilis), in the case of young children, into the mode of feeding, into teething, may in many cases be wholly omitted; otherwise they are asked incidentally, or at the end of the examination. No very exact rules can be given in this connection; many of the physician's questions appear to the patient to be prompted by mere curiosity, unimportant ones as very necessary, etc.

In the case of unconscious or irresponsible patients, or of young children, we must obtain the anamnesis from the persons around the patient.

The second part of the examination consists in the study of the present condition of the patient, the *status præsens*.

It is best to proceed in a systematic way to examine the various organs, in order to overlook nothing of importance. It is well to begin with an examination of the nutrition of the whole body, color, etc., of the skin. Then the temperature should, if required, be measured by means of the thermometer.

After this we proceed to the examination of special parts of the body, beginning with those which are most involved in the disease, or whose diseases are most important; the head (the mouth and pharynx inclusive), neck, chest, abdomen (also the genital organs), the extremities. The examination should conclude with a study of the secretions and excretions.

If the above procedure has been exactly carried out, it is quite possible, in the present state of our knowledge, to form an approximately exact notion of the condition of the patient's organs, in most cases of chronic disease, and developed acute diseases. Next to the exactitude of the investigation, its many-sidedness should be urged.

The art of diagnosis is only to be learned by long practice at the bed-side. In general terms, the process of drawing the most correct conclusion as to the condition of organs from the materials amassed in the examination, is the following: We recapitulate to ourselves in a brief way the most important alterations of organs which we have found; we try to recognize in these groups of alterations a resemblance to well-known pathological conditions. If such a resemblance is not readily made out, we proceed by what is called the method by exclusion; that is to say, we review in our minds all the diseases which these organs may suffer from, and judge whether any of them embrace the symptoms we have observed. In this way we reach the conclusion that in all probability the group of symptoms we have observed constitutes a certain disease, or is one of several. We must not allow ourselves to be influenced by the presence of a prominent symptom, for this may not always be caused by one disease (as the bronchial breathing of pneumonia), but we should weigh well all the possible causes of the sound, and conclude that there is pneumonia only when all the other symptoms and the course of the disease concur to prove it.

Experience teaches that certain conditions and morbid processes usually exclude one another. Thus in cases of tuberculosis we seldom encounter heart-disease; and whoever has a developed morbid state of the heart has almost acquired an immunity from tuberculosis. In the same way tuber-

culosis and cancer hardly ever coincide in one individual. In cases of strongly-marked deformity of the thorax (scoliosis and kyphosis) tuberculosis hardly ever makes its appearance. Among acute diseases, typhoid fever is the one most often excluded by other conditions: it seldom attacks pregnant and recently delivered women, and almost never those who have acute rheumatism or tuberculosis. *Herpes labialis* is very rare in typhoid-fever patients.

Other morbid processes are often conjoined. Tuberculosis is always united with bronchitis; gastric catarrh with nearly all severe acute and chronic disorders; *herpes labialis* often coexists with intermittent fever and pneumonia; acute rheumatism and heart-disease are not rarely conjoined, etc.

As in individuals, certain forms of disease combine upon a large scale in certain periods of time. Whooping-cough and measles, scarlet and typhoid fevers, scarlet fever and angina, intermittent fever and dysentery often occur contemporaneously.

GENERAL PROGNOSIS.

In practice there is conjoined to diagnosis what we call PROGNOSIS, or the foretelling of the COURSE, MODIFICATIONS, and TERMINATION of the disease. In this connection also there is little to be said in a general way. The very first inquiry usually is, whether the disease will terminate favorably or unfavorably, or whether the issue is doubtful: *prognosis fausta, infausta, anceps.* The next points are, if life be not in immediate danger, will the restoration be complete; and last, how long will the disease last.

Naturally these questions must be examined in a more special way; for example, when the prognosis is unfavorable it should be determined whether a chronic disease, a secondary affection, or death is to be expected.

We call SEVERE DISEASES such as threaten permanent injury to important organs, or death to the patient; MILD DISEASES, those in which, under ordinary circumstances, a complete cure is to be looked for. BENIGN DISEASES are those in which the appreciable group of phenomena indicates a surely favorable issue; MALIGNANT diseases are those into the course of which unforeseen complications easily enter, as scarlet fever.

The answers to these prognostic questions are to be shaped upon the participation of the general organism (fever, state of strength, etc.), upon the extension of the disease in the body, upon the value of the affected organ for the maintenance of life, upon the patient's age, upon the vigor of his constitution, upon the character of an epidemic, upon the possibility of employing the proper remedies, etc.

The correctness of the prognosis depends mainly upon the exactness of the diagnosis. If it be in a measure true that at the present time minuteness in diagnosis is carried farther than is necessary for therapeutics, it is not at all so for prognosis. For, he who has an obscure view of the condition of a patient will be surprised by many variations in the course of the disease, which a better-drilled physician would foresee.

DURATION OF DISEASES.

The duration of diseases is exceedingly various. Many end in a sudden catastrophe, lasting one or a few minutes; many others last hours and days, many weeks and months, some during a lifetime. Diseases which last but a short time are called ACUTE; those which last a long time, CHRONIC diseases; and some pass from the acute into the chronic stage.

At the present time a classification is made rather upon the basis of the usual duration of individual diseases, as, for instance, in the case of phthisis and rachitis, which usually last for years. The term acute is applied when these diseases run their course in a few months. Typhoid fever is spoken of as an acute disease, although in many cases cure is postponed beyond the fortieth day.

Acute diseases not seldom end in chronic states, and chronic diseases sometimes terminate in an acute manner.

Synonymously with acute and chronic, we often hear the expressions FEBRILE and NON-FEBRILE DISEASES. This is true of a good many cases, though many acute diseases are non-febrile, many chronic diseases febrile, especially in their later stages, many affections are at various times febrile or non-febrile (catarrh, syphilitic, or more seldom other cutaneous diseases). Many non-febrile diseases either disappear quickly or kill suddenly (cases of poisoning, hæmorrhage).

Finally we have the terms TYPICAL and NON-TYPICAL, used together with acute and chronic, such as exhibit a regular course, measurable succession of stages, and those with a variable, indefinite course, without a distinct tendency to cure or death.

The duration of diseases depends in a general way upon the causes. If the causes have acted in a transitory manner, the duration of the morbid processes is short. If the causes are connected with circumstances not easily altered, as mode of life, habitation, occupation, the disease is apt to last longer. If the active agents are poisons which have been absorbed in small quantities during long periods of time, a prolonged languishing state is threatened.

It is also to be observed that the more localizations a disease has, the longer it will last.

Besides, the length of a disease depends upon the nature of the alterations which accompany it. The majority of disorders of circulation, and inflammations, run in general an acute course. The more diseases vary from these types, and are accompanied by metamorphosis of tissues (fatty, amyloid degenerations) and new-formations proper, the more their course is, in general, chronic.

Lastly, in some tissues, as in bones, all diseases last a long time, because of peculiarities in modes of nutrition.

COURSE OF DISEASES.

Every disease runs a defined course. The changes in the circulation and nutrition, the functional disturbances, which appear from the beginning of an affection to its termination in a return to the normal state, or the death of a part or the whole of the organism, are limited in duration.

Occasionally the alterations subside very rapidly, in a few minutes or hours. This is especially likely to occur when we have to deal with the so-called functional disorders, or with variations in the blood-supply of single organs, and also in cases where only a small amount of organic change has occurred: as, for example, in anæmia of the brain (the usual cause of vertigo), in hyperæmia of the brain, of the skin, lungs, and other organs, in many forms of spasms, in attacks of pain, as well as in many febrile states (*febricula*, or *febris ephemera*); a stationary condition, in which the phenomena remain the same for long periods of time, without increase or decrease, is not met with in strictly speaking morbid processes, but in the so-called morbid states (monstrosities, defects, etc.), as, for example, in many paralyses, certain muscular hypertrophies, encapsulated parasites, scars, pigmentary deposits, etc.

The majority of diseases run a definite and generally easily traced course, which is either regular or irregular.

A REGULAR COURSE, extending over days and weeks, is met with in numerous surgical and internal diseases, in the apyretic as well as in the

pyretic. Besides, among these are some which exhibit periods regularly
succeeding one another, each period having peculiar characters, the so-called
TYPICAL or RHYTHMICAL (cyclical or periodic) diseases, such as many
apyretic affections (neuralgia, hæmorrhage, gout, etc.), and also, and
especially, certain pyretic diseases (typhus and typhoid fevers, relapsing fever,
small-pox, measles, scarlatina, common pneumonia, recent intermittent
fever). Other diseases are only approximatively typical, that is to say,
their course is on the whole not very regular, or only so during a part of
their duration, as in many apyretic catarrhal diseases, rheumatism, gout,
but particularly febrile affections and as many acute catarrhs, tonsillitis,
acute articular rheumatism, meningitis, pyæmia, erysipelas, etc. There are
yet other diseases which are non-typical, that is to say they exhibit during
their course a type which varies according to the severity of the attack,
while the febrile manifestations show no regularity, or are altogether want-
ing, as in many cases of suppuration, inflammations of the serous mem-
branes, diphtheria, dysentery, phthisis.

In typical and almost typical diseases we not rarely meet with irregular-
ities, or deviations from the regular course. These depend upon ætiological,
individual, external, accidental, or therapentical influences.

In diseases having a duration of several days, be they regular or not in
their course, the onset is often most various. Not rarely an individual,
hitherto perfectly well, is suddenly plunged into a severe complexity of
symptoms, as happens in cases of wounding and tearing of internal and
external parts, in certain spasmodic effections (epilepsy), many intoxications
(by acids, phosphorus), and infections (scarlet fever, small pox), all febrile
diseases which begin with a chill (pneumonia, tonsillitis, intermittent
fever, etc.).

In the majority of cases, however, the disease begins more or less insidi-
ously, and its development is not noticed by the patient. To this category
belong the majority of non-febrile diseases, and also many febrile affections
of the mucous and serous membranes, such as catarrhs, pleurisies, rheuma-
tism. The physician finds the greater difficulty in correctly appreciating
these cases, because the phenomena of onset are in great part or wholly
obscure. They consist usually in general *malaise*, prostration, restlessness,
loss of appetite, sleeplessness, shooting pains in various parts of the body.
In some cases, even after the most exact observation, the physician finds
nothing definite on the first and second days. These manifestations, even
in cases in which the principal morbid process exhibits itself in other parts
(as in the skin in the acute exanthems), are designated as the forerunners,
or PRODROMATA of the disease ; and the time during which they are observed
is termed the *stadium prodromorum*, or the premonitory stage.

Later on in the course of the disease the various phenomena increase in
intensity, or new ones appear. The course of a disease but rarely proceeds
uniformly forward and backward in stated periods of time. This is only
true of certain febrile affections, especially the acute exanthemata (small-
pox, scarlet fever, measles), in a few other infections diseases (typhus and
typhoid fevers, relapsing fever, pyæmia), in a few internal inflammations
(common primary pneumonia, tonsillitis, cerebral meningitis), in intermit-
tent fever ; not at all in chronic diseases, consequently we define a number
of so-called stages :

THE STAGE OF INCREASE, or of INVASION (*stadium incrementi*), which
in febrile diseases is also termed the PYROGENETIC STAGE.

THE STAGE OF HIGHEST INTENSITY (*stadium acmes, seu staseos*), in febrile
diseases known also as the *Fastigium*.

THE STAGE OF DECREASE (*stadium decrementi*), which in febrile diseases at the time of progressive diminution of temperature is called DEFERVESCENCE, and may take the shape of CRISIS, or LYSIS.

Between the stages of highest intensity and decrease, in many diseases, particularly in severe cases of typhoid fever, pneumonia, acute exanthemata, etc., we meet with an intermediate stage, or STAGE OF INDECISION, which is termed *stadium amphiboles*.

By the terms CRISIS, or RESOLUTION, we understand an improvement which takes place suddenly, in a few (4–24–36) hours, and which is accompanied by a sudden fall of temperature (from $2°$ to $5°$ C.), and in pulse-rate (from 20 to 60 beats), and also by the occurrence of sweating, sleep, urinary deposits, etc. This is strikingly seen in relapsing fever, croupous pneumonia, measles, etc., and in intermittent fever.

Immediately preceding the improvement there not seldom takes place, in many diseases, a short increase in the gravity of the symptoms, the so-called *perturbatio critica*.

Formerly under the name of CRISIS was understood the termination of a disease by the excretion of morbid products, and their expulsion from the body. To illustrate, it was thought that the opacity of the urine, produced by an excess of urate of soda (not a rare occurrence at the crisis time), represented the expelling from the body of a substance produced by the disease, the peccant material. This notion is in a measure not wholly wrong, as we to-day admit that there are in the secretions substances produced by deranged metamorphosis during the disease ; but we believe that these products are the results, not the causes of the disease ; and that the morbid condition does not cease because these are excreted, but that the substances are thrown out when the local disease improves. In a word, we to-day employ the word crisis rather in a symptomatological way, as an expression for certain appearances, not in an explanatory sense.

We speak of LYSIS, or solution of the disease, if the improvement (falling temperature and diminishing pulse-rate) lasts longer than two days, and yet is completed rapidly and permanently. This is observed in typhoid fever, scarlet fever, many catarrhal affections, etc. Occasionally, after all these stages have been gone through, the same morbid conditions appear afresh. At an early stage this return of disease is called RELAPSE, if it take place as a part of the disease, a phenomenon of its normal course (as in relapsing fever) ; if not, it receives the appellation of RECURRENCE. In a recurrence of a disease it is possible that not only the part previously affected be attacked anew, but other parts of the same tissues or organs as well, as, for example, in erysipelas, pneumonia, typhoid fever, pleurisy. The laity are also in the habit of using the words recurrence and relapse, as meaning complications arising out of the original disease.

All diseases do not, however, exhibit an uniform and stated increase and decrease of symptoms. Their course shows fluctuations, and even interruptions. These fluctuations, if they indicate an improvement, are called REMISSIONS, and if they consist in an aggravation of the symptoms, EXACERBATIONS. These phases are met with in many non-febrile, acute, and chronic diseases, and in some febrile affections (many chronic exanthemata, rheumatism, catarrhs, etc.). Attacks of illness which return from time to time, allowing complete intervals of health, are called periodical (as, for example, intermittent fever, epilepsy, nervous asthma, *laryngismus stridulus*, whooping cough). The period in which the symptoms make their appearance is called the PAROXYSM, or attack ; the normal interval, if in a febrile disease, is denominated AFYREXIA, or non-febrile period.

THE INTERMITTENT TYPE is sometimes regular and fixed, that is to say, the paroxysms return regularly at the same hour every day (as in intermittent fever) ;

sometimes it is irregular and changeable. The latter may occur in two modes. Either the paroxysm occurs each time one or more hours earlier than the preceding one, the *typus intermittens anteponens* (as at the beginning of intermittent fever), or it makes its appearance later each time, *typus intermittens postponens* (as toward the end of intermittent fever).

In intermittent fever there is always a regular rhythm, including periods of one or more days, and which is shortened on each day only by a few hours at the farthest. If the attack of fever returns every day we have what is called a QUOTIDIAN rhythm or type ; if something like forty-eight hours intervene between the beginning of two attacks, so that the fever recurs on the third day, we call it TERTIAN ; if the fever returns on the fourth day (interval of 72 hours) it is a QUARTAN. Cases with a more lengthened rhythm (up to 28 days) are very rare.

The word PAROXYSM is often used when speaking of remittent affections, when it is synonymous with exacerbation : in which sense we speak of paroxysms of dyspnœa caused by foreign bodies in the larynx, by polypi and croup. We often call paroxysms (vernacular, *fit*) affections which, though not periodic, occur at irregular intervals, as hysteria, gout, epilepsy.

In febrile diseases the following groups, with reference to the course of the disease, are distinguishable, though they often shade into one another.

THE SHORT FEBRILE DISEASES, the so-called attacks of fever (febricula, ephemera) which have a duration of two or at the most three days, ending in cure, and in which the temperature suddenly rises to 40° C. and over, and falls quickly, as in surgical and puerperal traumatic fever, in many catarrhal affections.

THE CONTINUED FEVER, which usually begins suddenly, is often ushered in by a chill, attains in a short time a temperature of 39°–40° C., shows small daily variations, and diminishes rapidly after several days, or often a fortnight (as in primary croupous pneumonia, scarlet fever, small-pox, typhus fever).

THE REMITTENT FEVER, which resembles the above in many particulars, but which usually exhibits a marked fall of temperature in the morning, and slowly ceases.

THE INTERMITTENT AND RECURRING FEVER, which shows periods of normal temperature between the moderately long paroxysms of fever : which character is especially well-marked in intermittent fever (ague) and in relapsing fever, less well-marked in pyæmia, erysipelas, and measles.

CHRONIC FEVER, which lasts for weeks and months, seldom uninterruptedly ; usually showing an intermittent or remittent form, as in pulmonary phthisis, in cases of internal or external suppuration.

The majority of febrile diseases only exhibit one type of temperature variations ; a very few showing several different types, as, for instance, intermittent fever, pneumonia, scarlet fever, typhoid fever.

All the above expressions, the determination of the so-called stages, depend exclusively, or in a great measure, upon observations of the course and progress of the fever. Such variations, with the exception of isolated disturbances of the circulation, are rarely observed in anatomical alterations ; these increase quite regularly and steadily, seldom with marked changes, either exacerbations or remissions, as in acute articular rheumatism, many cases of inflammation of the skin and mucous membranes, etc. At certain intervals gross changes in the tissues (inflammation or abscess) will, of course, occur ; but they do not appear externally in so decided a manner. Among intermittent diseases there are some which are non-febrile, most of them being pure nervous affections, as epilepsy, many forms of pain, mental affections. The last-named disease intermits as distinctly, though not in as regular a way, as febrile affections, and not rarely we can predict the week and day of recurrence.

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Hæmorrhages, next to fevers and spasmodic affections, exhibit a degree of regularity in their return : as hæmorrhage from the rectum, the lungs. The hæmorrhoidal flux is very apt, like menstruation, to assume a four-weeks' type. Gout exhibits, with tolerably clear intermissions, a tendency to recur in periods of one or two years, and oftener afterward.

It is at present impossible to give an explanation of these mysterious phenomena. In the case of hæmorrhage and gout it may be assumed that something having been discharged from the body during the attack, a rest will naturally ensue until the substance shall have accumulated anew. Epileptic and neuralgic outbreaks may also be looked upon as the relief of a tension, or as a discharge, though matters are not made clearer by this explanation. The well-marked rhythm of paroxysms of fever is also beyond our comprehension.

TERMINATION OF DISEASES.

Diseases may terminate in one of three ways:—
1st. By a complete return to the normal state—CURE or RECOVERY.
2d. INCOMPLETE RECOVERY; or the change into new morbid conditions—SECONDARY DISEASES.
3d. IN DEATH.

I. TERMINATION OF DISEASES BY CURE.

Complete recovery is usually heralded by the so-called period of convalescence, a period without definite limits, in which, though a degree of well-being has returned, greater or lesser weakness and sensibility to external influences remain. It is after severe acute diseases that the manifestations of convalescence are most clearly marked. The general sensations (*gemeingefühl*) of the patient are better, his disposition is hopeful and joyful. The animal appetites are aroused, but longing for food is chiefly shown. This want is justified, and nutritious food, appropriate to the power of digestion, should be furnished. After too hearty meals, or other errors in diet, the tongue easily becomes coated, or red and dry. Occasionally a slight fever makes its appearance during digestion. The intestinal evacuations are sometimes normal, sometimes constipated or free. The sexual desires are heightened, pollutions are frequent, and a tendency to onanism is occasionally observed. The other phenomena are those of anæmia. The heart, as a rule, beats slowly, though, at evening especially, the pulse-rate may rise because of slight exertion. The distribution of blood is at times abnormal, as is shown by sudden changes in the color of the face. Respiration is free, but easily made more frequent by the slightest movement. The temperature of the skin is normal, exhibiting the usual daily variations; but it rises easily in consequence of various external influences, little errors of diet, etc.; variations much greater and more easily produced than those observed in health. The skin is uniformly warm, though liable to sweating and refrigeration ; especially the feet are liable to become cold on first rising. The color is pale; and at times the epidermis comes off, even when no eruption has existed. The hair falls out, especially after typhoid fever, small-pox, severe puerperal fever, and also after other serious diseases, and even after diseases of moderate gravity. The subcutaneous connective tissue is devoid of fat. The muscles tremble after even slight exertions; they are in a state of mal-nutrition, and partly atrophied. The capacity for thought is diminished. The special senses are sensitive; after reading a short time, or after any small exertion, headache

appears. Sleep is in general good, although the patient is disturbed by slight causes.

CONVALESCENCE, as a rule, lasts a long time after most acute general diseases, after all diseases attended with high fever, large exudations, hæmorrhage, and suppuration. After typhoid fever, variola, scarlatina, many surgical diseases, etc., weeks and even months elapse before the patient regains his previous condition of nutrition, muscular and nervous power.

How does recovery take place? By what means are lesions made to disappear? Is there a natural cure, and an artificial cure? Is the patient cured by the physician, or does he, as it is commonly expressed, get well of himself?

First of all, it is a fact that a great many disorders disappear or at least may disappear, without the interference of the physician; this is the natural cure.

That many affections, particularly disorders of circulation and the slighter disturbances of nutrition, readily subside when their causes are removed, depends partly upon the fact that the body contains a great number of regulating and compensatory contrivances. The last are probably present in all systems, and are in part purely physiological, in part pathological. For example, if the external temperature rise, so that more water than before is thrown off from the skin and the lungs to the air, the amount of other excretions, the urine in particular, is thereby diminished. If the atmospheric temperature falls, the cooler air takes up less water from the surface of the body, this diminished evaporation of water is equipoised by an abundant flow of urine. In consequence, the amount of water in the body remains the same in either case.

We have in this connection three great groups to consider, which are distinguished from one another by the mode of union and the dependence of their elementary parts: the nerves, the blood and the glands, and the tissues in so far as they are contiguous.

COMPENSATIONS IN THE NERVOUS SYSTEM ensue either through nutrition, or by the transfer of the disorder to some other part. If a nerve be affected, and it begin to undergo the change from the pathological to the normal state, it may be, in the first place, that a stage of tranquillity and exhaustion succeeds that of irritation, just as in sleep, as if by a simple resting (recuperation) of the nerves. Or, it may be that through counter-irritation, that is through a new and stronger disorder, the interior movement of the tissue is increased, an increased metamorphosis is brought about. We see the same thing in exhaustion of the nervous system under the influence of irritating and exciting agents (wine for example). Or, it may be that the return of nerves to the normal state is brought about by a kind of saturation, similar to what occurs in health during the fasting state, in which more nutritious material is carried to the exhausted diseased nerves. In all these cases we have to deal with a greater tissue-change, whereby more old (effete) material is removed, and more fresh material added than before.

It is easy to refer to many compensations in the nervous system; some disorders of the nervous system become neutralized because the excitation as it extends from part to part is gradually exhausted by the resistance it encounters. For example, one can easily conceive the termination of an epileptic or hysteric convulsive attack. In many other cases the transition takes place with great irregularity, because different parts are differently irritable, and ganglia are interposed along the various paths. These not only cause changes in the direction of impulses, but also quantitative variations, increase or decrease.

After section of many nerves the function abolished by the operation returns without any reunion of the nerve; for example, as after the section of the splanchnic

nerve. The exact conditions of the restoration are unknown. In brain-injuries improvement may possibly be brought about by the assumption, by parts adjoining the lesion, of the properties of centrifugal fibres.

COMPENSATIONS IN THE BLOOD take place less in the blood itself than in those organs in which metamorphosis is most active; the glands for example.

A fault in the composition of the blood may affect the whole fluid, or, being partial, may involve the blood-corpuscles, the dissolved constituents (albumen, fats, salts). The repair is brought about by a limitation of the waste, or, as in convalescence, by the acquisition of new elements from the blood-preparing or assimilative organs. Increased consumption of blood elements in disease depends mainly upon the amount and extent of the local disorder, and upon the height and duration of the fever. The larger the ex-udation, the more degenerative processes or even hæmorrhages take place, and consequently the greater will be the diminution of the blood elements, especially the blood-corpuscles.

When the local process has proceeded only to a moderate extent, the im-poverishment of the blood is easily compensated by the addition of new ele-ments, providing the digestive and absorbing organs be in good condition. The restoration proceeds in part from the direct absorption of food intro-duced into the stomach and intestines (water, albumen, salts, fat), in a lesser degree by the resorption of substances stored away in the body (fat), and lastly, by the production of new histogenetic elements (blood-corpuscles) in the hæmatopoietic apparatuses (spleen, lymphatic glands, etc.).

A defect by excess in the constitution of the blood may not be simply a quantitative one, by the too great abundance of a normal ingredient, but may also be qualitative by the addition of a foreign element. The means of equalization are the same in either case. The superfluous substance is destroyed in the vascular system, often by oxidation or by reduction, or it is thrown out by the kidneys (bile-pigment), or by the skin or digestive tract (uric acid in gout, urea in many kidney diseases).

In this sense the old Hippocratic doctrine of critical excretions and critical local-izations has its justification, as well as the idea of blood-purification. It is even possible to defend in this sense the designation of blood-purifying remedies, in so far as these remedies specially increase excretion, and thus bring about the separa-tion (depuration) of certain substances from the blood.

It is not that all such excretion and separation of substances from the blood have a beneficial effect upon the course of disease; they often, on the contrary, become themselves the cause of new disorders. The pathological alterations of a part often directly become causes of new attractions and relations, and the organ thereby comes to play the part of an excretory organ for substances which were previously foreign to the part.

COMPENSATIONS IN TISSUES take place in two different ways.

If the tissues be filled with foreign substances, these may be removed by reflex movements (sneezing, coughing), by increased secretion (as in the nose, aërial passages, tear-ducts), or by and through the blood and lymphatic vessels (as serum, the colorless blood-corpuscles, and in part, also, the red corpuscles, foreign bodies deposited in the tissues, as dust, etc.). In this way many disorders of circulation and many inflammatory affections are cured.

At other times a true restoration is only brought about by the complex way of nutrition. The altered parts must not only be removed gradually, but must be replaced by new ones (muscular fibres, nerve-fibres, epithelium, glandular tissue).

Not rarely individual elements of tissues are wholly destroyed by the alterations which they experience. This does not always cause a cavity in the tissue. The cavities which may be formed are often gradually replaced by new tissue. This takes place very rapidly in epithelial structures, where the waste is usually a great one, and where pre-existing elements come up to replace the loss. In the deeper parts the restoration is so much the more difficult in proportion to the delicacy of the organization and the complexity of structure of the part. We know, for example, that the external skin and mucous membranes, with their glandular apparatus, are never wholly reproduced; and that in the place of the lost tissue a connective-tissue formation, having the characters of a scar, appears.

Particularly important for the organism as a whole, sometimes easy and sometimes difficult of explanation, is the neutralization of disease by the participation of organs bearing a relation to the organ first affected; the formation of a collateral circulation, the formation of connective tissue around foreign bodies, even parasites; the thickening of one of the bones of the forearm or leg after the excision of the other; the hypertrophy of one kidney when the other is atrophied or diseased; the hypertrophy of the left ventricle in insufficiency of the aortic valves; the hypertrophy of the right ventricle in various disturbances of circulation in the lungs, in disorder of the left *ostium venosum ;* the hypertrophy of organic muscular fibres in impaired calibre of affected hollow viscera, etc.

The more developed the nervous activity, the more free the circulation, the more intimate the normal combinations and connections of the anatomical elements, the more easy and complete the possible neutralization or natural cure of lesions will be. Natural or spontaneous cure, if we speak of it in the abstract, takes place only through physiological processes and through certain necessary ways.

PREDISPOSITION. plays some part in lesions of parts, and in the matter of compensation. A predisposition of a part to the starting of alterations shows that there already existed something morbid. It depends upon a degree of departure from the normal composition, which we do not, to be sure, recognize as a state of itself, but one by which the elementary parts are made of more unstable composition, and their destruction through retrograde metamorphosis made easy. The predisposition of a part to disease is in part congenital and inherited, in part developed by preceding morbid changes. For the abolition of predisposition the best means is physiological exercise, not merely of the part itself, but of all which are in relation with it.

Here habit, tolerance, and acclimation play parts. Through exercise, that is through repeated activities of a part, the operations of certain modes of activity are facilitated, which in their turn make the more rapid occurrence of equalization possible. Through the habit of certain influences, which coincides with a dulling of irritability, the operation of certain activities is retarded. Consequently, habit protects in a different way from exercise, by preventing the commencement of lesions. Acclimation acts in the same way.

In addition to the healing of nature (spontaneous cure), is there an artificial cure? This is a most important question for the physician, one which is before him all his life.

The answer to this question must in general terms depend upon the means which the physician has in his hands. It is to be remembered that these means must remain within the limits of physiological possibilities; that is, that they can only operate in the manner and directions which have been

indicated above. Artificial healing is not, in principle, at all opposed to natural healing. Sincere and enlightened physicians in all ages have always acknowledged that they were only the servants of nature, *ministri naturæ*. The problem of the physician consists in weakening and abolishing the predisposition, and in facilitating the neutralization of alterations which have already begun. The physician can, at any rate, do in both directions what would be done with difficulty or not at all without his interference; he can bring about many things in an artificial way which "nature" would not cause. The physician often makes use of more quickly-acting remedies than nature has at her disposal; he burns, ties, cuts away, enlarges narrow places, etc. Though this appears contrary to natural processes, yet it is not so in reality, since the same is seen, though much more slowly, in the extrusion of foreign bodies, the isolation of pieces of dead bone, etc. It not rarely is in the physician's power to decide whether he shall interfere forcibly or let things take their own course. In internal diseases analogous conditions are present: we can often, by means of expectorants, emetics, laxatives, etc., quickly bring about that which might otherwise have endangered life by occurring slowly. The use of cold, in the various forms of cold applications, sitz-baths, complete baths, etc., furnishes us with a means of reducing dangerously high temperature of an external or internal part, or of the whole body, by one or several degrees. And, further, operations upon the nervous system afford most excellent opportunities for the physician: he can bring about an early resolution of tension in the nervous system (by means of morphia, digitalis, bleeding, derivatives), he can so act upon nerves as to stimulate or paralyze them (acting upon the pupil by means of belladonna and Calabar bean, upon the cardiac nerves by digitalis, etc., and upon the vascular nerves by means of nitrite of amyl), he often can make irregular movements of the heart again regular (digitalis), etc. It is also possible to act upon the blood, as we can directly furnish materials for hæmatosis, and we can so regulate diet as to provide in abundance the ingredients needed by each individual case. Even upon the reconstitution of tissues we can in many ways exert a direct influence: by agents which facilitate resorption; by caustics, astringents, transplantations. The physician should regulate the external conditions and influences which operate upon the morbid state, he can set new external conditions in action, which without his interference would not come into play at all. In the special treatment of lesions it cannot be said that there is a blind experimenting with means; this would be neither in the interest of science, nor in that of the patient. The medical man has enough to do, if he makes use of earlier experience with due consideration, and every therapeutist who clings to the laws of natural science, and does not venture beyond the facts, must acknowledge himself to be a rational empiric in the treatment of disease. Pure empirics, that is, those who treat disease by past experience, without judgment in reality, do not exist. For, accurate conclusions are drawn even by the roughest analogy from the immediate exhibition of medicines. He who reflects, who takes one, two, three, or more circumstances into consideration, instead of one, when seeking an analogy, usually treats rightly.

Artificial healing is therefore not wholly identical with natural healing, but neither is it opposed to it. Artificial healing makes use of the tendencies and forces present in the body, and through them, by the help of more favorable circumstances, artificially produced, brings to pass the possible neutralization of lesions.

(See VIRCHOW, Allg. Pathol., pp. 15–25.)

II. TERMINATION OF DISEASE IN INCOMPLETE CURE—SECONDARY DISEASES.

A cure is said to be incomplete when there still exists a tendency to disease. It is not possible to indicate with precision the conditions upon which this predisposition depends; it must be upon changes in form and composition of parts; but such minute ones that they have, up to this time, escaped our means of investigation. We more particularly meet this predisposition after many inflammations of the skin, mucous membranes, the tonsils, lungs, and joints.

Contrarily, in many diseases a predisposition to recurrence is destroyed by a first attack, sometimes for a time, sometimes forever. This is more especially the case in infectious diseases, shown in the most striking manner in yellow fever, typhoid fever, small-pox, scarlet fever, measles. It is at the present time quite impossible to explain these facts.

INCOMPLETE CURE is distinguished from secondary affections by its being a remains of certain morbid conditions, whereas the latter consist of new morbid processes. Such conditions, which are not always referrible to distinct anatomical lesions, are, for example, paralysis of the extremities or of individual muscles; others, which do depend upon special anatomical conditions, are dislocations of bones, distortion of the skin, narrowing of canals by scars, twisting of the intestines by unnatural fixation of its serous coat; or others, which are partly anatomical and chemical processes, such as disorders of gastric or intestinal digestion, disposition to fluxes, etc. Or else, an entire organ, a limb, is and remains destroyed, as after ulcerative processes, after gangrene, etc.

The conception of SECONDARY AFFECTIONS is like the majority of medical conceptions, not easily made out in practice. For instance, secondary affections are often confounded with what are called COMPLICATIONS, that is to say, a succession of morbid processes, each one of which depends upon the others. In articular rheumatism we meet with inflammation of the pericardium, or endocardium, in about one-third of all cases. If this take place at the same time as the rheumatic attack, and if the physician discover it, he says that the rheumatism is in that particular case complicated with peri- or endocarditis. Often, however, the signs of the cardiac inflammation are indistinct or unnoticed during the attack of rheumatism, and it is only after the ceasing of the rheumatism that the cardiac lesion is made out, in which case it is customary to speak of the heart-disease as a secondary affection.

When we speak of secondary affections, we must make sure that there be a causal relation between the first and second diseases. Definite anatomical alterations must remain of the first disease, even though they produce no symptoms, or if the symptoms of the second disease are overlooked during the course of the first. In this sense pulmonary phthisis is not seldom a disease secondary to measles, habitual diarrhœa or constipation secondary to dysentery, etc.

Furthermore, a number of the processes termed metastatic belong to this category. In former times, by METASTASIS was understood the transposition of *materies morbi* from one part of the body to another. Most usually is this use of the term now restricted to the transfer of erysipelatous inflammation of the skin to the membranes of the brain, the swelling of the epididymis at the same time with cessation of the gonorrhœal discharge, the occurrence of inflammatory swelling of the testicle simultaneously with diminution of a parotid inflammation, the setting up of a cardiac or pericardial inflammation at the same time with the cessation of rheumatic joint-inflammation, the so-called metastatic inflammation in pyæmia.

III. TERMINATION OF DISEASE BY DEATH (THANATOLOGY).

Death is the suspension of tissue metamorphosis, its characteristic symptom is the cessation of the functions. It is necessary to distinguish local death, the death of a single organ, from general death. Even in general death the decease of individual parts of the body does not follow at one blow, but takes place successively. If the function of an organ or part is very important, we are soon made aware of its death; the death of the brain and heart is instantly recognized, while the loss of a kidney is ascertained only at the *post mortem* examination of the body, the death of the hair in typhoid fever first becomes noticeable during convalescence.

We still frequently hear it stated that one of the signs of death is that the dead parts undergo putrefaction, resolving themselves into simpler compounds; but this is in reality one of the consequences of death. This supposed character is, furthermore, not invariably present, as the bones and teeth are but slightly changed chemically in death; and besides, a nerve which is cut in the living subject is dead, and yet does not undergo decomposition. The cessation of life alone is not sufficient to burst the bond which holds the elements together in complex atoms; there must need be an impetus from without, that of heat, moisture, fungi, etc. And it is true that, as a rule, these do not fail, and we consequently have putrefaction as a sign of irrecoverable loss of life.

The transition from life to death may take place with absolute suddenness. In this strict sense death takes place only by lightning, sunstroke, bruising or lacerating, gunshot wounds, during birth and confinement, during severe operations, in many conditions of intoxication, and in certain enormous internal hæmorrhages (*apoplexia fulminans*); and this even in persons previously sound. In such cases it is noticed that the attitude of the body and the facial expression are just as they were in the last moments of life, as is testified by the bodies of suicides, and the bodies remaining upon the battle-field. In weakened persons, in convalescents from prolonged severe diseases, in certain diseases of the heart and brain, a similarly sudden mode of death has been observed.

In the vast majority of cases, however, death ensues in a more or less gradual manner; certain signs precede its occurrence, and foretell its approach. The stage in which these signs occur is called the agony or death-struggle. It is called a struggle because it sometimes takes place with symptoms of excitement, chiefly attacks of pain and spasms, and because it is intended thereby to designate in a poetical way the mutiny of the vital principle against impending annihilation. However, death not seldom comes quietly and noiselessly; it is the sleep of death, so common in very aged individuals. The strength of the body bears no relation to the kind of agony; the strongest subject of apoplexy slumbers unnoticed into death, while the most emaciated consumptive may struggle for days before terminating his existence.

The phenomena of agony are in nearly all cases made up of the symptoms proper to the disease which has caused the cessation of life, and of signs of progressive paralysis of the nervous and muscular systems. If palsy was previously present, it remains; or, if the disease was characterized by symptoms of irritation, these gradually subside. The mental faculties are usually diminished or suspended. The moribund, except in those rare cases in which consciousness is retained, is wholly indifferent to all his surroundings. Most usually consciousness is lost; sometimes it returns in the last moments, and there is relative quiet after pre-existing pain, etc., signs which are claimed to constitute the physical pleasure of the dying—

scenes which novelists and excitable relatives always relate with many ex-
aggerations (the last words of the dying, the so-called ecstasy, or *vaticinatio
morientium*).   The unprejudiced observer sees in the quietude the progress
of paralysis, the commencing loss of muscular tonus.

The various apparatuses die in a definite, somewhat regular succession.

If consciousness is preserved, the senses survive.   The sense of smell
and taste are the first to fail; then usually follows sight, and the dying per-
son not unfrequently complains of seeing fog, or calls for light.   The acous-
tic apparatus is still impressed by sounds when vision is quite dark, and
it is because of this that the persons present around the death-bed must be
warned against making indiscreet manifestations.   The sense of touch is
sometimes soon diminished, and sometimes it is the last to wholly dis-
appear, as the irritability of the conjunctiva for example.   The dying not
rarely feel the cold which is creeping up from below over the body.

Of the muscles, the external ones are the first to lose their property of
responding to the will; movements are tremulous, rather feebly convulsive;
sometimes more or less generalized muscular contractions occur without
producing any tension of tendons or movements of limbs; the body
slides downward in the bed, the limbs, in accordance with gravity, fall like
lead when raised up and let go; the facial lineaments are haggard, the lower
jaw droops, the eyelids fall down over the eyes without covering them
wholly, the axes of the eyes are parallel, the pupils usually small, though
becoming very large just before death; the conjunctivæ are reddened during
a prolonged agony; the eyeballs are no longer fixed, the cornea becomes
lustreless and flaccid; the temples sink down; the nose becomes pointed
and appears elongated; the outlines of the jaws become more evident
through the limp muscles; the chin appears more pointed and projected;
the lips are dry; the face yellowish, at times bluish, cool, often covered
with cold, clammy sweat—we have the *facies Hippocratica.*

The breathing becomes slow, infrequent, and laborious, the respiratory
movements are for the most part dissimilar, so that several superficial
movements follow a deep one; shortly before death they become still more
rare, and, with the exception of a few movements of hiccough, and of sigh-
ing, are very easy.   Nearly always the bronchial tubes are filled with
mucus, which cannot be expelled by cough; and we have at the end audi-
ble râles (the so-called death-rattle).   The throat is widely open, and the
œsophagus paralyzed, so that beverages fall into the stomach with a rumbling
noise.   The sphincters resist but feebly, and are easily overpowered by the
muscles of the viscera which are only relatively powerful, so that involun-
tary evacuations of fæces and urine in the bed are quite common.   Much
more seldom there occurs lachrymation, or an emission of semen or prostatic
fluid.

The contractions of the heart become unequal to the persisting tonus
of the arteries; the arteries are less and less filled, the pulse becomes
small, frequent, and at last imperceptible.   In consequence, the entire skin
loses its redness and turgescence; the face especially becomes suddenly or
gradually blanched, showing sometimes a tinge of yellow, except in case
of disorder in the lesser circulation, when it is usually bluish; the sebaceous
follicles are prominent; the hair and nails appear elongated.   The visible
mucous membranes usually are of the same tint as the face.   In fever-
patients the temperature often rises by .5° or 1° C. during the agony.   In
many cases the elevation is sudden and very great, especially in numerous
cerebral and infectious diseases.   In these cases it is also not rarely ob-
served that during a few minutes, a quarter of an hour, or even an hour

after the last breath, the mercury rises several tenths of a degree. At the same time the end of the nose and ears, as well as the hands and feet, usually feel cold. The contrary is observed in those cases in which the patient, affected with a pyretic or apyretic disease, exhibits in the agony a fall of temperature of 1° C., or more, below the normal. This is, for example, the rule in cholera, after severe hæmorrhage, in death by inanition.

An exact knowledge of the symptoms of the agony has not merely a theoretical but a practical value; enabling the physician to inform the relatives of the approach of certain death; to stop the giving of medicaments proper, with the exception, under peculiar circumstances, of anæsthetics (euthanasia); in Catholic countries to notify the priest; and also to make preparations for the performance of operations (the Cæsarean section for example).

It is difficult for the physician to state with precision the exact moment when death takes place. Usually a last breath is seen, consisting naturally of an expiration, and this is considered the end of life. But sometimes the respirations are toward the last most irregular, so that often after what seems the last respiration there occurs another noisy and groan-like, one-half to two minutes later; and even after this truly last breath signs of life are observed in other organs. If we open the chest of animals immediately after death, the heart is seen beating spontaneously. (The experiments of an English Committee showed that in asphyxia produced in dogs by the introduction of a tube in the trachea, the cardiac contractions lasted as long as three minutes fifteen seconds after the last respiration.) The arteries, before they collapse forever, drive the blood into the veins; in them and in the cavities of the heart where the blood accumulates the more, the longer the agony lasts and the more slowly muscular power fails, the fibrin coagulates. The flow of lymph may last one hour or more after death (BIDDER, LESSER). The muscles respond to electricity (*vide infra*); and if artificial respiration be performed in asphyxiated animals, voluntary movements return. If the abdominal cavity be opened, the muscular apparatus of the intestines contracts spontaneously, or by means of electricity, for several hours after death. That in the peripheral nerves the proper electric nerve-force survives awhile, is shown by the discovery of facts upon dead animals.

As long as manifestations of activity take place spontaneously, or can be artificially provoked, death is not general, and a general revivification is not impossible. If we define death as the definitive suspension of all vital manifestations, we must allow between the last breath and the total and irretrievable cessation of irritability an interval of time, during which life does not manifest itself by any phenomena appreciable to our senses, and in which we are to suspend judgment upon the question whether the subject belongs to the living or the dead. If a sick person has exhibited all the above described signs of agony, it can be safely said that after the last breath the rest of the organism will soon wholly die. The cardiac contractions soon cease after breathing has been arrested, and then there is naturally a stoppage in the transport of oxygen to the tissues, to whose activity this gas is indispensable.

JOSAT (*Sur la mort et ses caractères*, 1854) calls this passage of life into absolute death *mort intermédiaire*, and describes several cases in which it was prolonged as long as twelve hours. According to von HASSELT (*Die Lehre vom Tode und Scheintode*, I., 1862) many cases of apparent death belong to this class of phenomena.

By the term APPARENT DEATH we understand a condition in which all manifestations of life, if not altogether absent, are so reduced to a minimum that the affected person bears a most extraordinary resemblance to a corpse. It is only by careful observations that there are discovered a slight inspiration, a feeble cardiac contraction, a hardly noticeable and transitory muscular contraction, especially about the face, eyes, and lips. Consciousness and sensibility, and even animal heat, are hardly or not at all recognizable, and

the sense of audition alone is sometimes normal. This deathlike state may endure for hours and days. The possibility that a minimum of vitality will suffice to prevent the decomposition of organic matter, we see in plants during the winter time, in the pupa state of insects; most marked, however, in hibernating animals.

The following varieties of apparent death have been defined in accordance with causes :

1. Apparent death in consequence of internal morbid states: deep syncope after extreme fatigue from long marches, after extremely severe labor, rarely after prolonged hunger (shipwrecked and insane persons); severe spasmodic, hysterical, epileptic, and eclamptic seizures; catalepsy and lethargy; the asphyxial form of Asiatic cholera—many forms of yellow fever, the plague, typhoid fever; tetanus; convulsions in children; prolonged paroxysms of nervous asthma, and angina pectoris.

2. Apparent death from external impressions: extensive and severe contusions after corporeal punishment; a high degree of concussion of the brain, especially after powder explosions; severe or numerous wounds, particularly those accompanied by much shock or great loss of blood ; frequently after severe hæmorrhages, in puerperal women and small children.

3. Apparent death from specific causes: apparent death from breathing irrespirable gases ; apparent death of the newly born ; apparent death from drunkenness, hanging, and strangulation, from freezing, from rarefaction of the air, from compression, or from burial under earth, from foreign bodies in the mouth or pharynx ; apparent death from lightning-stroke, from heat, from narcotic intoxication (opium, hydrocyanic acid, chloroform, volatile carbon compounds). Occasionally several of these causes co-operate.

The lesser grades of apparent death, those in which consciousness is preserved while the ability to perform movements is suspended, are seldom met with ; they are most frequent after poisoning with curare, nicotin, chloroform, protoxide of carbon.

The apparent death of the newly born (*asphyxia neonatorum*) is of the greatest practical importance. SCHULTZE defines this condition as an asphyxia of the child born living, one developed in the uterus, and one which may be interrupted, not leading inevitably to a fatal termination. The causes of this condition, produced by asphyxia, by impeded placental respiration, are partly in the fœtus, partly in the maternal organism ; among the principal are : premature separation of the placenta, compression of the umbilical cord, hæmorrhage, pressure on the brain ; of less importance, are : too long duration of labor after the escape of the waters, too long duration of individual pains, too short intervals between pains, spasm of the uterus, hæmorrhage on the mother's part, apparent death of the mother. Some children, apparently born dead, show a turgid, purplish skin, injected and often protruding eyeballs, their muscles are inactive though their tonus is but little or not at all diminished, the vessels of the cord stand out full of blood, the umbilical arterial pulse is more or less slow, usually full. Others exhibit a pale, faded skin, relaxed muscles (hanging down of the lower jaw and the limbs, palsied anus), the umbilical vessels are narrow, their pulse small, infrequent, or altogether wanting. In the first defined class the respiration usually is absent, in the second it is usually present, though rare and jerking. The former are called apoplectic, the latter anæmic apparent deaths.

(Compare B. S. SCHULTZE, *Der Scheintod Neugeborener*, 1871).

Apparent death is of especial interest, because of the possibility of the subjects of it being buried alive. This occurrence is possible with early burials (in some countries six hours, in others twenty-four hours after death), and when the verification of the death is neglected or carelessly made.

The dread of being buried alive is based first upon a series of cases, in which patients, considered as dead, have come to themselves just previous

to interment; second upon the fact that individuals condemned to die by
hanging have come back to life after execution; and lastly upon the facts
that supposed corpses have shown signs of life after the commencement of
an autopsy, and that women have shown such signs after the Cæsarean sec-
tion.

The greater number of cases of burial alive are not well established, and
the various circumstances brought forward as proofs of the fact can be
otherwise explained; this being true of the unnatural position of the corpse
in the coffin, noises heard in the vault, mutilation of the fingers, apparent
growth of hair, etc. It would seem that *bonâ-fide* cases of this kind are
very rare.

The dread of being buried alive is an awful one, and yet there is in truth but
little basis for the fear. This is not because of official verification of the signs of
death, etc., for that is very imperfectly carried out in cities, and particularly in the
country; but because the cases are rare. The subjects are usually newly born chil-
dren, drunken, or hanged men, or it occurs in cases which have, previous to the ap-
pearance of seeming death, surprised physicians and laymen by their remarkable
symptoms. It is chiefly among women of hysterical, insane, cataleptic disposition
that we meet with cases in which the subjects can lie for one or even two weeks exhib-
iting a cold, pale skin, rather fixed eyeballs, hardly perceptible pulse, very faint
cardiac sounds, and hardly recognizable respiratory movements. Frequently in such
cases the consciousness and hearing are intact, the patients feel their painful situa-
tion, but are unable to give any manifestation of activity; remembering afterward
all that transpired round about them. Such cases undoubtedly do occur, but the
number of those worthy of credit is very small (SKODA, *Zeitschr. d. Gesell., d. Wiener
Aerzte*, VIII., p. 404; ROSENTHAL, *Wien. med. Jahrb.,* 1872, p. 397. Compare also
the cases collected, the majority without criticism, by BRUHIER, FONTENELLE,
BOUCHUT, BRIQUET).

The measures for the prevention of premature burial are: the prohibiting of early
interments (usually, not sooner than seventy-two hours after death), careful watch-
ing of the body in the room where it lies before burial, or in dead-houses; and where
this cannot be done, obligatory inspection of the corpse, or obligatory autopsies.

(Compare besides von HASSELT, GUST. LE BON, *De la mort apparente et des inhu-
mations prématurées*, 1866. FAURE, in *Archives générales*, 1869, Janvier.)

The means of distinguishing apparent from real death, and which may
also serve in part as attempts at resuscitation, are the following:

The respiratory and cardiac movements continue in a very feeble way in
apparent death, not at all in real death. Great reduction of these move-
ments also occurs in deep morbid sleep and in syncope.

In order to demonstrate the breathing, we hold a down feather or a light
before the nasal apertures, or we place a small glass containing water upon
the epigastrium, and observe the oscillations of the fluid, or we hold a cooled
mirror before the mouth and observe if its polish be tarnished. These
tests are, however, by no means absolutely certain.

In order to observe the cardiac movements auscultation of the heart for
several minutes is to be recommended. In a number of cases of syncope,
asphyxia of the newly born, cholera, etc., this yields a negative result,
and yet restoration takes place. Besides, it should be remembered, that
in the living the cardiac movements may be interrupted for a short time
by artificial means; or, by acupuncture of the heart's apex we note whether
any movement be communicated to the needle; or, lastly, we try to ascer-
tain whether the circulation continues in the arteries or veins.

(MIDDELDORPF's *Akidopeirastik, Zeitsch. f. klin. Med.*, 1856, VII. *Prag. Viertel-
jahrs.*, 1857, III.)

We are not to place too much reliance upon the failure of the arterial pulse, for
this sometimes occurs during the agony while the circulation is still active; the

sphygmograph might be used to give surer indications of a remains of arterial con-
traction. DANIS (*D'un signe certain et immédiat de la mort réelle*, 1869) claims that
the emptiness of the arteries is an infallible criterion of death, and proposes as the
best means of determining this, the exposing and dividing of the temporal artery.

It is well in such cases of suspected false death to place a ligature firmly on a
limb, when, if the death be real, no turgescence of the veins will ensue ; and if the
veins are then opened no blood, or only a few drops, escape. As regards venesection,
it is a means of secondary value, as the flow of blood may also cease in simple syn-
cope. It is well in all cases to put on ligatures after venesection ; remembering,
however, that in corpses the development of gas may then force out a small amount
of blood. MAGNUS (*Virchow's Archiv*, 1872, LV., p. 511), advises that a finger should
be tightly bound with a thread ; in apparent death a slight redness appears in the
whole of that part which is beyond the thread, while in real death no such effect
ensues. Punctures may be made in parts where the small vessels have thin cover-
ings, the lips or tongue, and the escape of a few small drops of blood is a sure (?)
sign of apparent death.

Muscular irritability is excited by irritating sensitive nerves ; by pow-
erful light, by sternutatories, tickling of the nose, of the skin, burning
(mustard preparations, blisters, dropping of hot sealing-wax, of hot water,
application of the actual cautery), sprinkling with cold water, rubbing of
the entire body, particularly of the back, to excite respiratory movements.
The most certain means consists in the examination of the electrical excita-
bility of the muscles and nerves ; this disappearing, according to recent
investigations, in from one and a half to three hours after death.

Electricity has been long known and used as a means of testing for real death.
Compare NICOLAS, *De var. vaporibus mephit.*, etc., 1781. KITE, Ueber v. Michaelis,
Ueber die Wiederherstellung scheinbar todter Menschen, 1790. CRÈVE, *De metall. inita-
mento veram ad explor. mortem*, 1793. FOTHERGILL, *A New Inquiry into the Suspen-
sion of Vital Action*, 1795. HEIDMANN, *Zuverl. Prüfungsmittel zur Bestimmung des
wahren Todes*, 1804. STRUVE, *Der Galvanodesmus*, 1805. Later, the researches of
BOËR, KELCH, BICHAT, NASSE, and others are worthy of note. We refer lastly to S.
CRIMOTEL, *De l'épreuve galvanique ou bioscopie élect.*, 1866. ROSENTHAL (*Wien. med.
Jahrb.*, 1872, p. 389) has recently investigated the *post mortem* electrical excitability
of the muscles and nerves. According to these researches the time of disappearance
of excitability varies between one and a half and three hours after death ; it disappears
sooner after chronic than after acute diseases, more quickly in those reduced than in
the strong. The excitability of nerves fails sooner than that of the muscles ;
the orbicularis palpebrarum remains longest excitable. Even three hours after
death, when the rectal temperature is still 38 –37° C., when the joints are still flexi-
ble, the diagnosis of real death may be positively made from the loss of muscular and
nervous excitability to the faradic and galvanic currents. In a case of hysterical
seeming death, the preservation of electro-muscular and nervous excitability indi-
cated life when hardly any other sign of it was perceptible. Rosenthal considers as
erroneous the observations of Tracy and Josat, to the effect, that in ether sleep
and poisoning by carbonic oxide, the electro-muscular reaction is in greater part or
wholly lost.

The testing of the sensibility of the skin is not always certain, for there
are many cases of apparent death in which recovery takes place where,
owing to asphyxia, the sensibility to cutaneous irritants seems wholly lost,
and the same is observed in cases of deep narcosis produced by chloroform
[ether], hypnotism, etc.

A good means of testing real death is by applying mustard plasters, or
rubbing the skin with moistened flannel, or with brushes, until the
epidermis is destroyed. In cases of real death the spot on which lay the
mustard does not become red, the rubbed parts do not become moist, but
dry, and appear in from six to twelve hours yellowish brown, horny, and a
little translucent.

(KLUGE, *De cutis exsiccatione, certo mortis signo*, Lips., 1842.   E. H. WEBER, *Fro-riep's Notiz.*, 1858.)

HASSELT (loco cit., p. 31) cites several cases in which during the asphyxial stage of narcotic poisoning the skin was not reddened by the application of irritants, and in which, after the lapse of some hours, when some improvement had taken place, a blush appeared.   If the actual cautery be applied upon a corpse, there arise only carbonized, brownish, dry, more or less hard or leathery welts; at least no vesicles and no inflammatory reaction appear as in the living and in those seemingly dead . this constitutes CHRISTISON'S test.   According to JOSAT and BOUCHUT, there are some forms of seeming death in which all local reaction fails to appear under the cautery test; and in more recent times the reliability of CHRISTISON'S experiment has been much put in doubt by the experiments of BUCHNER, ENGEL, MASCHKA, and others.

The flexor muscles overcome the extensors (the arms are turned inward, the hands bent, the thumb thrust into the palm); the lower jaw hangs down; the sphincter ani remains open; the body flattens itself where it lies : all these things take place in true death.

BLUMENBACH attributes great value to the flattening and wrinkling of the skin.

The face of the corpse usually presents a pale, waxy appearance.   The face is purplish when death has occurred from a severe disturbance in the lesser circulation (strangulation, hanging, suffocation, drowning, severe pulmonary affections, especially in young individuals).   The face is yellowish in patients who have had icterus, etc.   People who usually have red faces sometimes preserve this color in death.   The finger-tips usually are of the same color as the face; sometimes they are bluish in bodies which are otherwise pale.

The skin of the dead is wholly opaque, that of persons apparently dead not so. This last is best seen by holding one's own fingers held close together against a bright light ; the sides of the fingers appear reddish and translucent.   The non-translucency of the fingers (so-called dynamoscopy, of COLLANGUES) sometimes fails in cholera patients, in the subjects of hectic, while it may be present in those dying of dropsy.

Discolorations, *livores mortis*, are purplish spots which in general make their appearance in from eight to twelve hours after death ; at first upon dependent portions of the body, in the dorsal decubitus upon the back of the corpse, upon the face, belly, and chest, if the corpse have lain upon its face.   Later, with the progress of decomposition, they extend over the whole body.   They are the more extensive in proportion as the blood is more fluid (suffocation, infectious diseases).   Their color depends upon the color of the blood : they are very pale when the blood is poor in blood-corpuscles, bright-red in poisoning by carbonic oxide, bluish-red in cyanosis, etc.   Body-discolorations are by no means a conclusive sign of death : they have several times been seen during life in cases of asphyxia by charcoal vapor, in which recovery took place ; and in such cases they are present upon the anterior as well as the posterior surface of the body. In very anæmic and in dropsical subjects they are occasionally wholly absent ; in many cases (scarlet fever, typhus) they much resemble the petechiæ seen during life.   Occasionally these discolorations are very much like extravasations in or under the skin : an incision in the affected part serving to prevent this mistake.

The coldness of the body, *algor mortis*, appears at a variable time (one-half to twenty-four, a mean of six to twelve hours) after death, according to the temperature of the dying person and of surrounding media, depend-

ing, for instance, upon the stay of the corpse in bed, or out of it, varying in death from freezing or drowning. In very old and very young persons, in those who are extremely emaciated, and in the subjects of chronic diseases, it appears more rapidly than in younger and better-nourished individuals, and in those having acute diseases. In cases of hanging, in persons killed by lightning and by charcoal vapors, this condition sets in very slowly. In many forms of apparent death, as well as in asphyxia from freezing and drowning, and in the algid stage of cholera, the surface is extremely cold. (*Vide infra*, on FEVER.)

The eyelids are half open in death, very seldom closed. The eyes are sunken and their axes stand parallel. The eyeball is less firm, because some of its fluid contents has evaporated, and later because of the commencement of decomposition. The eye is wholly insensible. In a few hours after death the sclerotic becomes, especially if the eyelids are not closed, yellowish by drying; and later it seems to be covered with bluish specks, particularly in the neighborhood of the cornea; it becomes thinner and allows the choroid to show through it. The cornea loses its brilliancy soon after death, and becomes cloudy, in part because the intra-ocular tension is diminished, in part because of the loosening and swelling of its epithelium. A muddy appearance of the cornea does occasionally show itself just before or in the agony. A prolonged brightness of the eye is observed in cases of *apoplexia fulminans*, in death by strangulation, charcoal vapors, alcoholics, chloroform, hydrocyanic acid. The pupils are very wide and immovable.

LARCHER (*Archives gén.*, Juin, 1862) claims that the cadaveric infiltration of the eyeball is an important sign of death. It consists at first simply in a barely visible black spot, which extends more and more, usually of a round or oval shape, seldom triangular. It appears always in the white of the eyes, at first in its external, later in its internal side. Both spots extend horizontally, becoming narrower, and at length unite in the inferior segment of the eye. This cadaveric infiltration of the eye is a symptom of putrefaction; it is a transition state between the slightly marked, disappearing, or already gone, *post mortem* rigidity, and the well-known results of putrefaction.

The *post mortem* rigidity, CADAVERIC RIGIDITY, or *rigor mortis*, constitutes one of the most characteristic, though not absolutely certain signs of death. It commences in the muscles of the lower jaw and neck, then extends to the trunk, to the arms, and the legs, and at last involves the internal parts (the heart, vessels, stomach, intestines, etc.), diminishing in the same sequences. It makes its appearance sooner or later, according to the course of death ; most rapidly after many gunshot wounds, after drowning in cold water, after tetanus, after poisoning by hydrocyanic acid, and by strychnia, after high *ante mortem* temperature, sometimes after typhoid fever ; in general terms, the sooner, on the one hand, the more the muscular power was exhausted before death, so that we see after gunshot wounds, after tetaniform spasms, muscular contractions passing into rigidity ; on the other hand, after prolonged muscular inactivity, as in typhoid fever. Furthermore, rigidity appears sooner and is stronger in aged persons, in muscular subjects, after many very acute diseases. External influences, for example the long stay of the body in a warm bed, especially a very high or a very low external temperature, have but little influence, or none at all, upon the rapidity or slowness of the appearance of *rigor mortis*. Usually it appears in from four to twelve hours, seldom later than twenty-four hours, rarely in a few minutes, or immediately after death. *Rigor mortis* diminishes after it has lasted twenty-four to forty-eight hours, seldom earlier ; it occasionally per-

sists five to six days, as in death from acute poisoning by alcohol, and by nitro-benzine. In this condition the muscles—flexors as well as extensors—shorten and thicken, just as in contraction during life. The limbs are, owing to the greater strength of the flexors, somewhat flexed, the lower jaw, if it have hung down, is closed again, so that the face has once more a life-like aspect. Cadaveric rigidity invades also the non-striated muscles. The rigidity of the muscles of the skin is the cause of the so-called goose-flesh of the dead.

According to LARCHER (*De l'imbibition cadavérique du globe de l'œil et de la rigidité musculaire*, etc., 1868) the first muscles which stiffen are those which move the lower jaw, the muscles of the lower limbs almost simultaneously, those of the neck next, and last those of the upper extremities—be the cause of death what it will.

ROSSBACH (*Virchow's Archiv*, XLI., p. 558) has described a *rigor mortis* beginning during the last moments of life. In ordinary cases death completely relaxes the muscles, even if during the last minutes of life they were strongly or feebly contracted. In a few rare cases, however, the *post mortem* rigidity is a direct and sudden continuation of living muscular contractions. In such cases the attitude existing during life is preserved in death. This extremely sudden rigidity is met with after unexpected and sudden as well as after gradual death; it affects tetanized as well as feebly contracted muscles; it is not produced by special wounds; but besides in cases of gunshot wounds, this sudden stiffness takes place after tetanus, after drowning in cold water, after the injection of various medicinal substances into the arteries.

The living contracted muscle is translucent, soft, contractile, and very perfectly elastic; whereas the muscle, in a state of *post mortem* rigidity, is opaque, hard, non-contractile, inelastic, easily torn, and when once forcibly stretched does not again shorten, but remains soft. Living muscular fibres exhibit protrusion of the muscular substance through lacerations of the sarcolemma; dead ones do not. The cause of the stiffness is well known to be the coagulation of the muscular substance, myosin, which is liquid in life. In this coagulation a free acid (the so-called muscular milk sugar) appears; while the living muscular fibre, still fresh enough to respond freely to the galvanic current, always yields an alkaline reaction; free acid being found, without coagulation of the myosin, only in very much exhausted muscles. Myosin is coagulable in consequence of cessation of afflux of blood, by a temperature of 50° C. (the so-called heat-rigidity), by acids, especially carbonic acid. The restoration of fresh blood to rigid muscles does not, or does only in the least degree, make them again contractile, but they become decomposed. In solutions of common salt, of saltpetre, and carbonate of soda (which redissolve the coagulated myosin) rigid muscular fibres again look like fresh ones, but remain non-excitable. If, now, arterial blood be supplied, the muscular fibres once more become soft and translucent, exhibit an alkaline reaction, and contract after irritation of their nerves, as well as upon direct excitation.

Compare the physiological researches of HARLESS, BRÜCKE, DUBOIS, KÜHNE, and others. Also, ALBERS, *Deutsche Klinik*, Sept., 1851; KUSSMAUL, *Prag. Vierteljrschr.*, 1856, I., p. 62; and in *Virchow's Archiv*, XIII., p. 289; PELIKAN, *Beiträge z. gerichtl. Medicin*, Würtzb., 1858.

The considerations brought forward against the positive meaning of *post mortem* rigidity are of little value. The confounding of this condition with the muscular rigidity of apparent death in cases of freezing, of hysterical asphyxia with simultaneous catalepsy, with tetanic and eclamptic attacks, is hardly possible. That in many cases rigidity is not observed is in part owing to its being overlooked, in part because of its sudden appearance and disappearance, in part because of its late beginning. It is only in the prematurely-born fœtus, and in frozen and thawed bodies that it seems really to fail. This may also be the case in poisoning by mushrooms, in death by hydrosulphide of carbon.

In cholera-cases there have often been observed, several hours after death, movements of the legs, bending of the knee, raising of the arms (DIETL, and others), ejaculation of semen (GÜTERBOCK, and others).

The beginning of decomposition (putrefaction) coincides with the ending of rigidity. The ammoniacal products of this decomposition first neutralize the acidity of the stiffened muscles, and then dissolve the myosin.

Putrefaction is characterized by the cadaveric odor, by the greenish hue of the skin, and by the development of gases. These phenomena appear at a variable time (from a few hours to one week or more) after death, according to the temperature and moisture of the air, according to the composition of the body, the kind of illness which killed the patient, the degree of muscular irritability just before death; in general, it occurs soonest in plethoric and fat individuals, in newly confined women, after death from very acute disease; most slowly in old persons, in the emaciated, after chronic diseases, in those dead of alcoholism, etc.

According to BROWN-SÉQUARD, the period of commencement of both rigidity and putrefaction, as well as their duration, are immediately related to the degree of muscular irritability existing at the moment of death. Everything that diminishes the degree of muscular activity before death, determines a rapid development of rigidity, shortens its duration, and affects putrefaction in the same way; while everything that increases muscular activity acts in just the opposite way. Thus it is that animals hunted to death in an arctic winter become quickly rigid, and rapidly putrefy. The flesh of over-driven cattle soon spoils after slaughtering. In all cases of death by convulsions, rigidity and decomposition soon occur, whether disease or poison have caused the death. Everything which exhausts the system and reduces muscular irritability retards putrefaction. (See BROWN-SÉQUARD's *Croonian Lecture*, 1861.)

The cadaveric odor is characteristic. The greenish color first shows itself upon the belly, in the ileo-cæcal region; next in the intercostal spaces; and last in the remainder of the body; following by preference the course of the veins. It appears in a time after death which varies according to the temperature of the air to which the corpse is exposed, and according to the season; on the average upon the third day, though not rarely much later when the surroundings are cold. The occurrence of putrefaction is postponed if the body lies in an atmosphere containing watery vapor, and at 20° to 25° C. In colored people the greenish color may be recognized by rubbing the epidermis from the belly by means of a cloth. The green color is in all probability due to a combination of the coloring matter of the blood with sulphur.

The formation of gas begins in the intestines, distends the abdomen, and may then cause the lower bowel, the bladder, and even the uterus and seminal vesicles, to expel their contents after death. It afterward affects the entire skin, producing a raising of the epidermis by greenish vesicles.

Cadaveric rigidity and putrefaction in the first place, *post mortem* discoloration, the eye-ball changes, the kind of disease preceding death, and the agony in the second place are infallible signs of death. Although the first-named phenomena occur, under ordinary conditions, several, or many hours after death, it is, in individual cases, hazardous to make them the criteria of true death soon after apparent dissolution.

Besides those above enumerated, a great many means of distinguishing true from seeming death have been proposed. Of those some are not more reliable than those spoken of above, some are complicated and costly, some are really ludicrous. Such are NASSE's *Thanatometer*, VON HENGEL's *Abiondeictys* (indicator that no more life is present), MEYER's *Biometer* or *Bioscope*, the *cercueil musical*, etc.

Compare especially FR. NASSE, *Die Unterscheidung des Scheintodes vom wirklichen Tode*, 1841. v. HASSELT, *op. cit.* GAUNAL, *Mort réelle et mort apparente*, 1868.

The CAUSES OF DEATH are numerous ; but the following division may be recognized :

CESSATION OF THE CIRCULATION, through various diseases of the heart and great vessels.

CESSATION OF RESPIRATION, through the action of various causes (suffocation or strangulation).

DEFICIENT NUTRITION, either produced by albumen (*vide infra*, inanition), or by water (so-called water-inanition) ; the weakness of old age.

EXTREME OR LONG-CONTINUED ELEVATION OR DIMINUTION OF THE TEMPERATURE OF THE BODY, and simultaneous deficiency of regulating means (burning, freezing ; many diseases).

SEVERE PHYSICAL AND CHEMICAL AGENCIES (crushing, sun-stroke, lightning-stroke, etc.), and many poisons, some derived from without, others from within the organism (biliary acids, purulent infection, etc.).

SEVERE PSYCHICAL IMPRESSIONS (fright, grief, etc.).

Those organs which are the instruments of the most important activities of life, and whose injury most quickly causes death, were called by the ancients *atria mortis ;* they are the heart, lungs, and the brain, or, to be more exact, the medulla oblongata. Hence we have, especially for the laity, three different modes of death : (1) death from the brain, called death by apoplexy (as in concussion of the brain, large extravasations) ; (2) death from the respiratory organs, by asphyxia, or, more properly, by suffocation (as by the breathing of irrespirable gases) ; (3) death from the heart, by syncope (as, for example, in rupture of the heart). These three modes of death seldom, and only in sudden death, occur in pure forms. Usually, especially in slowly produced death, they combine with each other in various ways : for example, interference with the circulation alters the composition of the blood, and disturbs the circulation in the central nervous system, and this in its turn impedes respiration, and both together diminish the heart's activity. In individual cases, even when a well-conducted autopsy is made, it is often difficult to determine the exact way in which death has been brought about. Even where we have the most striking anatomical changes it is not easy to specify the immediate cause of death. We see patients die with pneumonia, typhoid fever, pleuritic exudations, articular rheumatism, etc., in whom the gross anatomical alterations are most probably as developed as in those cases which terminate in recovery. The morbid process by itself, *i.e.*, the intestinal lesion in typhoid fever, the infiltration of a pulmonary lobe, etc., does not usually kill. Many diseases go on to a fatal issue because of mechanical accidents, or complications not to be diagnosed. At the present day the greatest importance is attached to the anatomo-pathological condition, while the chemical processes are only regarded in cases of common poisoning, and in a few so-called constitutional diseases. And yet such processes must have played an active part in those cases in which the autopsy yields the so-called " negative results."

Although it is true that we cannot always say in what manner death was brought about, yet certain it is that the immense majority of human beings who die bear within them some severe tangible lesion. Nine out of ten men die of disease. Even in the still-born there are found numerous fœtal diseases, and in cases of " death from old age," there are usually important lesions aside from the quasi-normal alterations of organs produced by age. About as many persons die of acute as of chronic diseases. In hospital patients, among whom every form of disease is met with, there is about 1 death in 10 cases. Even under the most favorable circumstances

the proportion of deaths is 1 : 30.   The relation of deaths in a given period of time to the population during the same period, varies so much in different countries that we have 1 death to 20 or 50 lives ; children and still-born infants being included.

The following are the ratios in various countries :

ENGLAND, 1 : 51.
GERMANY, 1 : 45.
BELGIUM, 1 : 43.
SWITZERLAND, 1 : 40.

FRANCE, 1 : 39.7.
UNITED STATES = 46.3.
ITALY,   }
GREECE, } 1 : 30.

TURKEY, 1 : 30.
RUSSIA, 1 : 27.
BATAVIA, 1 : 26.
BOMBAY, 1 : 20.

· In large cities the mortality is greater than in the whole country in which they are :

DRESDEN, 1 : 27.7.
BERLIN, 1 : 25.5.
PRAGUE, 1 : 24.5.
VIENNA, 1 : 22.5.
LONDON, 1 : 46.7.
LIVERPOOL, 1 : 36.1.
MANCHESTER, 1 : 34.9.
GLASGOW, 1 : 35.
EDINBURGH, 1 : 37.7.
DUBLIN, 1 : 34.6.
PARIS, 1 : 47.4.
LYONS, 1 : 37.7.
NICE, 1 : 31.4.
NAPLES, 1 : 28.

ROME, 1 : 24.6.
FLORENCE, 1 : 28.
AMSTERDAM, 1 : 37.6.
COPENHAGEN, 1 : 42.2.
BRUSSELS, 1 : 44.2.
ATHENS, 1 : 30.3.
GENEVA, 1 : 51.5.
ALGIERS, 1 : 29.7.
ALEXANDRIA, 1 : 15.7.
CAIRO, 1 : 12.2.
NEW YORK, 1 : 30.6.
PHILADELPHIA, 1 : 38.3.
BROOKLYN, 1 : 34.1.
ST. LOUIS, 1 : 48.7.

CHICAGO, 1 : 36.1.
BALTIMORE, 1 : 39.8.
BOSTON, 1 : 32.7.
CINCINNATI, 1 : 48.6.
WASHINGTON, 1 : 49.0.
NEW ORLEANS, 1 : 32.7.
SANTA FÉ, 1 : 58.1.
PITTSBURG, 1 : 36.1.
RICHMOND, 1 : 34.9.
MONTREAL, 1 : 26.8.
BURLINGTON, VT., 1 : 102.0.
DENVER, 1 : 119.0.

[From N. Y. Board of Health Report for 1872.—ED.]

With the exceptions mentioned at p. 24, men do not die suddenly.   Thus we distinguish certain modes of death as very rapid or sudden, from the common death.   The end of life may still be said to occur suddenly, even when the death-struggle has lasted several hours.   What is essential in the conception of this mode of death (*mors subitanea, s. per apoplexiam*, in the old, symptomatic sense of the word) is the unexpectedness of the event relatively to the previous condition of the individual.   The symptoms of agony last from a few minutes to a few hours, consisting often only in insensibility, insomnia, convulsions, and difficult breathing.   A rapid death is frequent in the earliest years of life, is very rare from the first year to complete puberty, then increases in frequency with each year of life up to the fiftieth, and also occurs in the most advanced age.   It is once again as frequent in males as in females.   It occurs more frequently in the day than in the night ; and is more common in winter and spring than in other seasons.   Sudden death is more apt to take place shortly after meals, and during defecation.

If we take the mass of cases of sudden death in the symptomatic sense, and inquire what lesions are found in their examination *post mortem*, we may divide the total number into four categories :

1. Frequently no important alterations from which the fatal result might have come are found, at least none discoverable with our present means of observation.   This is true in many conditions enumerated above, further, in many cases of *commotio cerebri*, of crushing of the chest or abdomen, in operative or manual reduction of hernia, in cases of ovariotomy unattended by much loss of blood, and lastly, in cases of death from strong emotional disturbance.   Many cases of this kind are at the present time called cases of shock.

2. There are lesions which may be the cause of sudden death, and which are, in all probability, developed during the short agony.   To this class belong considerable serous effusion in the ventricles of the brain, extreme emphysematous distention of the superficial parts of the lungs, anæmia and

hyperæmia of the brain and the lungs. To this category also belongs, probably, the existence of free gas in the vascular system, without operation, and without a trace of putrefaction. Cases of this kind are met with in newly delivered women, in nursing women, in newly born and in very young children, in old and in very corpulent persons.

3. There are met with lesions which must positively have produced death in a short time; acute serous exudation in the air-vesicles (*œdema pulmonum*); the presentation of polypoid excrescences of the mucous membrane in the larynx; foreign bodies or solid exudations impacted in the larynx; entrance of air into the large veins, as may occur in operations; lacerations of the heart or great vessels; rupture of the stomach, liver, uterus (the peritonitis following these accidents only proves fatal after several days); severe cerebral hæmorrhage, bursting into the ventricles, or directly pressing upon or destroying the pons Varolii or the medulla oblongata.

4. There are found lesions which often kill, but which have lasted a long while, and it is impossible to say, from the conditions present, why death should have occurred just at that particular time. Independently of sudden deaths, we must, in this category, make the same interpretation which we must often fall back upon in cases of chronic as well as many of acute disease. Thus we meet with a sudden end in pulmonary tuberculosis, in the pneumonia of the insane or of old people, in diseases of the heart, in aneurisms, in cerebral softening, and tumors of the brain; only rarely in cholera, typhoid fever, the acute exanthemata.

Upon the subject of sudden death there is quite a large literature, both in the olden time (LANCISI, *De mortibus subitaneis libri duo*, 1707); and in recent years, compare especially HERRICH and POPP, *Der plötzliche Tod*, 1848.

PART SECOND.

GENERAL ÆTIOLOGY.

Compare the previously mentioned works on general pathology, especially those of HEUSINGER, HENLE, STARCK. Among newer works, REICH, *Lehrbuch der allgemeine Ætiologie u. Hygiene*, 1858, and *Ueber der Entartung d. Menschen*, 1868; STAMM, *Nos-ophthorie*, 1862; OESTERLEN, *Handb. der med. Statistik*, 1865; J. RANKE, *Grundzüge d. Phys. d. Menschen*, 1868 (2d ed.), and VIERORDT, *Grundriss d. Phys. d. Menschen*, 1871 (4th ed.). The special literature is indicated in each paragraph.

ÆTIOLOGY, or the knowledge of the causes of disease, is one of the weakest chapters of pathology. And this is because there are but few diseases of which we know a certain influence must of necessity have caused them; as is the case with many mechanical causes of disease, with parasites, poisons, medicines. Even in the few cases in which we do determine the operation of such an influence, as in the case of poisons, we remain ignorant of the nature of the substance producing the result; as in variola and syphilis. We only know that pus taken from a person having a given disease, if brought in contact with a healthy person, will produce a similar condition. And still we have as yet been unable to isolate the special poison.

What we know about the causal conditions of internal diseases is not for the most part about causes in the strict logical sense of the word, about *causæ sufficientes*, which of themselves must under all conditions produce a definite effect, but is about complex conditions, under whose influence, with more or less frequency, certain diseases appear. From a strictly scientific standpoint we must at once reject a large part of medical ætiology, because it is uncertain, undemonstrated, only half true; but from a practical point of view it is of the utmost importance to know everything which may by any possibility call forth disease—a knowledge indispensable if we would avoid disease.

From a rightly conceived ætiology flows in a natural way the PROPHY-LAXIS of disease. There are connected with ætiology two doctrines bearing close relations to one another; HYGIENE, which teaches how to preserve health, and THERAPEUTICS, which teaches how the diseased organism or the diseased organ may be restored to the normal state.

Every agency of nature, and every activity within the body itself, is a cause of disease the moment it possesses or acquires the power of disturbing the normal current of life. Consequently, the number of causes of disease is unlimited; and we can only bring to our cognizance the most important and most common ones. The same influences and irritations which are necessary to keep the organism in its normal condition, may conduce to morbid states by their extreme force. The conception of perniciousness is therefore quite as relative as that of disease.

A number of the pernicious influences which affect the organism operate only in a preparatory way, as *causæ remotæ*, PREDISPOSING CAUSES; that is to say, they themselves cause only small deviations from the normal state, which, however, the cause continuing to act, maintain a disposition to further disease—the basis of disease, or *dispositio ad morbum*.

This predisposition is not a mere pathological notion, as there is also a physiological predisposition.

That there are numerous individual differences with regard to the influence of various causes of disease, is very certainly established, for we not rarely see a number of men exposed to the action of similar morbid influences, exhibiting disease in varying form and intensity, or even having different diseases. This is most striking in the case of poisons, particularly mineral poisons; many men become sick after only a few months' exposure to lead, while others may be exposed for many years without suffering. The same seems true of scarlatina, syphilis, and malaria.

That caution should be used in stating this of the above-named diseases, is shown by the fact that it was formerly claimed that some individuals enjoyed immunity from tape-worm.

The predisposition to disease is a general one to which all organisms without exception are subject (for example, any human being may be crushed by a falling rock, or poisoned in an atmosphere of carburetted hydrogen) ; and it is also a special condition (for example, many men never get a miasmatic or contagious disease; nursing children are seldom the subjects of contagious diseases).

There is, furthermore, a certain degree of susceptibility to the various influences and irritants which act more or less continuously upon the organism. This susceptibility varies much in different individuals, and under different conditions. A too great degree of susceptibility is called erethism ; a too small degree, torpidity ; two conceptions which cannot be further defined, which are obscure, and yet are indispensable for the necessities of practice.

Predisposition to disease passes into disease proper by insensible gradations : such conditions are called sickliness, weakness, susceptibility, irritability. This heightened predisposition is often a more serious thing than true disease ; the subjective state being often much better after a threatened disease than before it. The morbid disposition may, furthermore, subside without any actual disease having developed from it. It is seldom destroyed by the occurrence of a disease ; it is more often only suspended for a while ; sometimes it is lengthened. This predisposition evidences itself chiefly in particular organs and systems, as for example, in the skin, the intestinal mucous membrane, the respiratory organs, etc. These parts, having a striking liability to disease, are called *partes minoris resistentiæ.* The organs predisposed to disease in general, or to special diseases, show either no abnormality, or an anatomical or histological alteration.

Whether there have been predispositions or not, the system is usually assailed, before the beginning of a severe disease, by another external influence, which is known as the proximate, occasional, or exciting cause, *causa proxima.* This consists either in a single morbific influence (wounds, shocks, poison), or in a complex group of influences (as, for instance, "taking cold"). It further happens that many diseases appear only after the cause has been acting several days ; and that probably in the majority of affections causal influences are at work which escape our observation. All these reasons dispose us, like laymen, to connect an illness with any coincident occurrence, without our being able exactly to determine the relation between the two.

What relation exists between predisposing and exciting causes is wholly unknown. In general terms they stand in an inverse relation : that is to say, the stronger the predisposition, the slighter the exciting cause needed to develop a disease, and *vice versa.*

If the predisposition be so strongly marked that disease is produced by

the operation of exciting causes which are of a strictly physiological character, we have to do with individual susceptibility or IDIOSYNCRASY. To this class belong the instances of urticaria developed after smelling of or eating strawberries, after eating lobsters, etc., of headache produced by tobacco-smoke, of sneezing from the inhalation of a small quantity of ipecacuanha, etc. ; probably also the production of hay-asthma (*catarrhus æstivus*) during the haymaking season.

The predisposition to disease is often wrongly appreciated. It is either confounded with an early stage of the disease itself (as in the falsely so-called phthisical and apoplectic habit), or, what is more frequent, with the exciting causes of disease (as in the matter of the greater frequency of fractures and of pneumonia in men).

Whether there be any of the so-called cumulative effect in the causes of disease—that is to say, whether the frequent or long-continued action of one cause will ultimately produce a more extensive or more intense affection, cannot be determined at present.

That there is such a thing as resistance, or becoming habituated to morbid causes, is not to be doubted. This is most certain about certain poisons, as is shown in the case of the arsenic-eaters of Steyermark, of alcohol-drinkers, opium-eaters, workmen in lead, smokers and snuffers of tobacco. The same is probably true of many contagious poisons and miasmata. Among all other causes of disease, this is most strikingly exemplified by the habit of enduring great variations of temperature.

We cannot now give any explanation of this resistance power. It is partly comparable to the immunity of certain animals to the action of certain poisons, which are more frequently vegetable and animal than mineral. We can imagine that either the morbid cause is made harmless immediately at the spot where it is received, or that after its entrance into the blood it is quickly separated by secreting organs (liver, kidneys).

Causes of disease in general are either internal or external ; in other words, they are such as lie in the individual, or such as reach him from without.

I. INTERNAL CAUSES.

1. INHERITANCE.

LOUIS, *Sur les maladies héréditaires*, 1748. ROUGEMONT. *Abh. über d. erbl. Krankheiten*, *Uebersetz. von* WEGELER, 1794. PIORRY, *De l'hérédité dans les maladies*, 1840. LUCAS, *Traité de l'hérédité naturelle*, 1847. MOREL, *Des dégénérescences de l'espèce humaine*, 1857.

Children often exhibit defects or diseases which one or both of their parents had before them. This fact becomes comprehensible when we reflect upon what takes place in the lower animals. In such of the lower animals as multiply by transverse or longitudinal segmentation, each individual of the new generation is literally a half of an individual of the preceding generation. Each half must of necessity equally share the anomalies of form and composition existing in the whole individual. And in those animals, a part of which after separation from the parent is developed into a complete animal by the formation of new organs, it is still conceivable enough that abnormalities of the original creature should descend to the scion. Now it must be remembered that ova and semen in the higher ani-

mals are nothing else than parts separated from the paternal and maternal bodies, both contributing to the development of the new being. The fact of inheritance from the father is made even clearer by new observation, showing that spermatozoa are not merely brought into close contact with the egg, but penetrate it through the micropyle. These considerations show that the actions of modifying activities may extend to the descendants, and must do so; but they do not explain why a certain disease of the generator is reproduced in the young.

The influence of sexual relations with an individual will exert an influence upon the maternal organism which occasionally lasts beyond the confinement. There are, for example, cases on record of negresses, who, after having had children by white men, have born mulattoes in wedlock with negroes; as well as of children descended of white parents, and bearing traces of colored blood, their mothers having previously had mulattoes by negroes. In the domestic animals we meet with much more numerous and more striking instances of the same kind. For example, a slut of pure race impregnated by a bastard dog does not bring forth bastard young on that one occasion, but is not for a long time capable of producing, with a pure-blooded male, a truly pure-blooded progeny; her young are always a little imperfect.

We must always recognize various conditions in inherited and congenital diseases; such as the influences derived from the father and mother, which existed before the act of procreation (true inherited or conceptional diseases); as the influences depending upon the condition of the parents during generation; further, what may have been experienced by the fœtus *in utero* (intra-uterine diseases); and lastly, what may have been impressed upon the individual by the family life, in part by the dwelling, etc., in part by similar habits, by similar education, etc.

1. The condition of the parents before generation is of great importance for the offspring. In order the better to realize the possibility of inheritance of disease, we should consider the transmitted similarities in physiognomy, color of the iris, intellectual capacity, which are apparent either very soon after birth, or later. Just as in one family an aquiline nose, and in another a pug nose returns, so there is inheritance of many malformations, as supernumerary fingers, hare-lips, cleft-palate, peculiar forms of ear muscles, phymosis, hypospadias. Even warts and mother-marks (pigment stains) occasionally re-appear in the same spot in children of those having them. Among true diseases, not only are the so-called constitutional diseases, as tuberculosis, syphilis, gout, lepra, diabetes mellitus, the hæmorrhagic disposition, or polysarcia, inherited, but also mental disorders, epilepsy, hypochondria, hysteria, and cretinism. Ichthyosis and the hæmorrhagic disposition, together with many malformations, such as hypospadias, show the peculiarity of re-appearing only in the male descendants: so that the daughters, themselves free from the diseases, transmit them from grandfather to grandson, to their own sons. Cataract is especially transmissible in the female line, tuberculosis, gout, polysarcia, etc., nearly always appear in the children for the first time at the age when these diseases are most common: for example, the children of phthisical parents remain often perfectly well till their twentieth or twenty-fifth year, when they break down rapidly, and are, as a rule, more severely affected than are those who acquire tuberculosis; certainly many die in the first year with pulmonary or meningeal tuberculosis. It not seldom happens that at the time of procreation both parents appear healthy, though one of them, issue of a tuberculous family, already carries the germ of the disease, to use a figurative expression; the children may become tuberculous. Further, the inheritance is not always of the very same lesions. If the parents have become the subjects of secondary syphilis, their children

often die in the womb, and the fœtus is ejected before the end of pregnancy as a putrefying body ; or the children die in the first few weeks of life, of simple wasting ; or they live, and later become scrofulous ; or, lastly, they in their turn become syphilitic. Drunkenness in the father not rarely causes mental disease in his descendants. It is a matter of common experience, that in families in which insanity is hereditary we meet with examples of the greatest intelligence, and with epileptics and imbeciles. It is still more remarkable how often two perfectly healthy parents will have healthy children with malformations and defects.

In the well-established instance of KÜHN (*Schriften der Berlin. Naturf.*, 1870, Bd. I., p. 367), two healthy parents, derived of healthy families, gave issue to five children. The oldest son, aged 24 years, was 3 ft. 2 in. high, with very small generative organs, without sexual appetite, was the subject of cataleptic attacks ; the second child, a son, 21 years old, large, like the former in respect to sexual development, was simple-minded and mischievous ; the third child, a girl 16 years old, 3 feet high, an imbecile; the fourth, a girl aged 10 years, and the fifth, a boy of 7 years, both imbeciles. There are many such examples on record.

Women affected with secondary syphilis bring forth syphilitic children. Contrarily, those having tertiary syphilis bear for the most part healthy children, even when the disease is very severe. Attempts to inoculate tertiary syphilis fail.

As offsets to such sad results there are a few considerations. Inasmuch as male and female fluids combine for the formation of the germ, the embryo may be constructed in its various parts after the fashion of one or the other parent ; in so much as it takes after the father, it is less like the mother, and *vice versa ;* so that by a preponderance from one side the influence of the other may be counteracted. The mingling of stock is a means of preventing the degeneration of succeeding generations ; while it is well known that the intermarriage of relatives tends to develop family traits and diseases to an extreme degree. It is especially known in the case of cretinism and idiocy that the marriage of related persons favors their appearance, while it is prevented by marriage among persons of different races and countries. The same is true in a lesser degree of deaf-mutism. Other remarkable facts are the frequency of sterility in related couples, and the uncommon mortality of children of such parents. And yet we meet with remarkable exceptions to these rules.

The intermarriage of relatives is followed by sterility and abortion on the one hand, and diseases (weakness and malformations of all kinds) in the descendants on the other. A committee, presided over by Dr. Morris,* of New York, published the following table in 1859 :

Relationship.	Families.	Number of Children.	Perfect Children.	Defective Children.	Percentage.
Third cousins.......................	13	71	42	29	40.8
Second cousins	120	626	360	266	42.5
First cousins	630	2,891	955	1,936	66.9
Cousins offspring of cousins.	61	187	64	123	65.7
Uncle and aunt, with niece and nephew............................	12	53	10	43	81.0
Double cousins.....................	27	154	21	133	86.3
Incestuous	10	31	1	30	96.7

According to Voisin, the mental and bodily health of the 3,300 inhabitants of Batz (Loire inférieure) is uncommonly good, although owing to its location on a strip of

* This table is by Dr. Bemiss, of Kentucky, for the whole United States, and was quoted by Prof. A. W. Morris. Morris' paper is in Trans. of the New York State Medical Society, 1867, p. 351.—ED.

land almost as isolated as an island it is the scene of frequent intermarriages. Malformations, mental diseases, idiocy, deaf-mutism, epilepsy, etc., are wholly absent, as well as sterility and a tendency to abortion. Voisin denies the evil influence of marriage between relatives, if the participants enjoy good health and have a strong constitution.

With the question of the influence of the parental condition upon the health, etc., of children, there is closely allied a number of questions, whose solution is of the greatest practical importance. Which sex has the greater influence in generation? To what circumstances is it owing that sometimes the father, at other times the mother exerts a prevailing influence? Are the dispositions of the father and mother more readily transmitted to the sons or daughters? Are the peculiarities in certain organs and systems in the latter developed more especially under paternal or maternal influence? These and similar questions can receive only a partial solution at present. We need upon these points observations, and experiments upon animals. In the breeding of cattle it has been universally recognized that the offspring especially resemble the father. In the human species, it is believed that the mother's influence prevails.

Furthermore, it is desirable to determine the actual frequency of inherited diseases, not their necessity. We frequently see dwarfish animals or deformed human beings giving issue to perfectly normal offspring. In the case of certain special diseases, tuberculosis and syphilis, it is on the whole but seldom that the children of diseased parents remain well. It must be remembered that the embryo has only the tendency to disease, and that through favorable influences its development may become normal.

2. Too much importance has been attached to the influence of the accidental condition of the parents during procreation. Great stress has been laid upon the moral disposition of aversion or indifference, of intoxication during the sexual act. It should be remembered that at the time of copulation the semen and ovum have been for some time fully developed, and only undergo transportation at that time. That debility, age, habitual drinking, etc., should enfeeble the germ is evident; the state of the parties during coition can have influence upon fertility only by helping or preventing the contact of semen and ovum.

3. During intra-uterine life a number of so-called inherited imperfections and diseases arise, caused in part by infection of the fœtus by the mother, and in part by independent fœtal diseases. The latter may be designated congenital diseases in contradistinction to inherited diseases.

It being assumed that the father has been healthy, the child can only be infected during this period by the mother. During pregnancy everything that is transportable in the mother's blood may be carried to the fœtus. In this way the mother's anæmic state may harm the child; syphilis and small-pox, seldom scarlet fever, measles, dysentery, typhoid fever, intermittent fever, puerperal fever, even tuberculosis and cancer, may be communicated to the fœtus. The fœtus may experience several affections, small-pox, for example, without the mother's participation. It is different with the mental state of the mother during pregnancy; it is doubtful if mental depression, insanity, etc., can affect the already formed embryo through the blood.

In this category belong the so-called impressions of pregnant women, whose possibility cannot be completely denied on *a priori* grounds. Yet many of the cases cited in support of this causal influence are fœtal diseases. (W. A. HAMMOND, *Influence of Maternal Mind over the Offspring during Pregnancy and Lactation. Journal of Psychological Medicine*, 1868, p. 1.)

A great number of malformations, particularly those through arrest of development, are referable to fœtal diseases. The embryo has his vascular system, his own nutrition, just like an adult; and consequently there may

occur in him, just as in the adult, blocking up of a given vascular region, effusions of blood, exudations, atrophies, hypertrophies, etc. For example, it has been demonstrated by complete series of preparations, that the encircling of an extremity of fingers by turns of the umbilical cord, or by threadlike false-membranes, may eventuate in true spontaneous amputation. Furthermore, we meet with cicatrices, closures, atrophy, dropsy, etc., in the embryo, in parts which, in the born child, cannot undergo the same processes, because death would precede them. This holds good of many malformations of the brain and medulla oblongata, of closures (atresiæ) of the mouth, throat, intestinal canal, etc., of many pulmonary (syphilomata) and renal diseases. Contrarily, we occasionally observe in the fœtus, as well as in the grown individual, slight lesions, causing great disturbances, especially if they involve undeveloped organs. For "if the needed size and regular quality of the embryo-organ be wanting, the resulting adult-organ becomes shrunken or defective." Malformations arising in this way are either simple defects, or they are instances of arrested developments. In either case, the part is very imperfectly or not at all developed. Growth proceeds only to a certain point. Usually it is impossible to make out a special cause for the greater number of such malformations. It is only rarely that it is satisfactorily shown that mechanical agencies (blows, etc.) have acted upon the fœtus. Malformations have been produced experimentally by wounding the ovum. This shows that only a part of malformations are explicable by fœtal disease.

4. Seeming transmissions are sometimes classed with inheritances, as, for example, many habits of walking, of movements in general, of handwriting; and also abnormalities which children acquire in later years from association with the parents, by the force of imitation, such as certain eccentric mental traits, hysteria, etc.

5. Lastly, children become sick in the same manner as their parents, because they are surrounded by similar external influences, such as similar dwellings, similar food, similar sources of infection.

2. AGE.

See QUETELET, WAPPÆUS, ZEISING. Also special treatises upon the diseases of newly born, nursing, and older children, by VALLEIX, 1838; MAUNSELL AND EVANSON, 1838; RILLIET ET BARTHEZ, 3d ed. 1861; REES, 1844; BOUCHUT, 1845 and 1862; LEGENDRE, 1846; BEDNAR, 1850, 1851; GERHARDT, 1861 and 1871; HENNING, 1855 and 1864; WEST, 1857; A. VOGEL, 3d ed., 1867; STEFFEN, 1855–1869; STEINER, 1872. SCHREBER, Die Eigenth. d. kindl. Organismus, 1852. Works on diseases of old age, by CANSTATT, 1839; DURAND-FARDEL, 1858; GEIST, 1860; METTENHEIMER, 1863; CHARCOT, 1868.

The periods of life, or ages, are: 1. The NURSING AGE, from birth to the irruption of first teeth (7th to 10th month); 2. CHILDHOOD, from the first teething to the second dentition; 3. BOYHOOD, or GIRLHOOD, from the second dentition to puberty (14th to 15th year); 4. ADOLESCENCE, from puberty to the complete development of the body (21st to 25th years); 5. EARLY MANHOOD, from the 25th to the 45th year; 6. LATER MANHOOD, from the 45th to the 60th year; 7. OLD AGE, from the 60th or 65th year onward.

According to WAPPÆUS, in 10,000 individuals the ages are divided as follows:

0 to 5th year,	1,120.	20th to 25th year,	887.	50th to 60th year,	846.
5th to 10th "	1,066.	25th to 30th "	806.	60th to 70th "	548.
10th to 15th "	933.	30th to 40th "	1,373.	70th to 80th "	250.
15th to 20th "	941.	40th to 50th "	1,107.	80th to 90th "	58.
				Over 90th "	5.

With respect to age, there are to be considered : 1. The probability of becoming sick ; 2. The mortality at different ages ; and 3. The predisposition to certain special morbid states.

1. MORBILITY, that is to say, the probability of becoming sick, is very great in the first week of life, greatest in comparison to that in other periods of life ; it diminishes after the sixth week, though remaining great until the end of the first year. After that age it progressively diminishes until the seventh or eighth year. From the eighth to the eighteenth year disease is once more more frequent ; it again gets rarer with the complete development of the individual, reaching a second minimum between the twenty-fourth and thirtieth years. From that age to the end of life the liability to disease goes on increasing.

The statistics upon this point are liable to several objections. In statistics there should be a similarity of conditions, a similar mode of life, and similar occupations. Or, at least it is necessary to be acquainted with all the diseases of a given territory. Usually, however, the maladies found in hospital patients are studied in connection with numbers of the population ; a fact which explains numerous inaccuracies. According to VILLERMÉ (*Ann. d'hygiène*, II., p. 247), a male of the working class, aged 20–30 years, is sick on the average 4 days in the year ; one of 35 years, 4½ days ; one of 40 years, 5⅓ days ; one of 45 years, 7 days ; one of 50 years, 9½ days ; one of 55 years, 12 days ; one of 60 years, 16 days ; one of 65 years, 31 days ; one of 67 years, 42 days ; one of 70 years, 75 days. FENGER (*Quid faciunt ætas annique tempus ad freq. et diuturn. morb. hom. adulti.* Havn., 1840) states the same proportion for the period from the 20th to the 30th year, though he does not find that morbility and the duration of sickness are greater in the succeeding years—they only begin to rise in old age. FENGER based his conclusions upon observations made upon the marine workmen (*Flottenhandwerken*) of Copenhagen, a corps having a military organization ; he takes into account the subjects of syphilis and wounds ; and wounds are especially liable to occur in the most robust.

2. MORTALITY does not bear any exact proportion to the frequency of disease ; since it depends mainly upon the degree of danger attending each disease, and this again differs at various ages. The mortality-records of different localities and states differ even when the disturbing influence of epidemics is eliminated. The estimation of the average duration of life, or of probable survival at every age is of general and practical importance for societies, widows' pension associations [*Wittwenkassen*], life insurance policy, and for the State.

The average duration of life, calculated from mortality-tables (the number of years which all the dead have attained is added up, and the sum divided by the number of the dead) is as follows in different countries (the still-births being excluded).

AUSTRIA....... 28.19 yrs.	SAXONY........ 31.16 yrs	ENGLAND....... 36.92 yrs.
SARDINIA..... 30.80 "	BAVARIA...... 32.61 "	FRANCE .... 40.36 "
PRUSSIA...... 31.10 "	NETHERLANDS. 34.72 "	NORWAY........ 43.64 "
		UNITED STATES. 24.1 "

The number of still-births amounts to 4 per cent. The causes of still-births consist in foetal diseases, as well as in diseases and unfavorable conditions of the mother before and during confinement.

Tables of mortality are almost perfectly in accord upon the following points, viz., that mortality is disproportionately great in the first month of life, that it decreases from the second month to the end of the first year ; and that from the second year it diminishes rapidly, reaching a minimum between the eighth and twentieth years. The death-rate is small between the twentieth and the forty-fifth years ; it is more especially so between the ages of twenty-seven and forty than immediately before or after. After

forty-five the mortality increases, though slowly. At the fifty-fifth year it again reaches the proportion it has at five years; at the seventieth year that it has at three years; at the eightieth year that of the sixth month; from the ninetieth to the ninety-fifth year it amounts to the rate at the second month, and at the one hundredth year it surpasses the rate during the first month.

Mortality-tables (so-called life-tables) are tables which indicate the death-rate of a population or generation ; that is to say, mark the order in which a certain number of persons born simultaneously, or of persons of a given age, die from year to year. They equally show the probability of death, the order of dying, and the probability of survival (probable duration of life) for each year of life. For example, the following table of mortality for Belgium, by QUETELET.

Age.	Population : Number Living.	Deaths in 10,000.	Probable Duration of Life (years).	Probability of Death.
0	10,000	1,503	41.56	0.1503
1	8,497	615	50.58	0.0724
2	7,882	299	53.28	0.0379
3	7,583	196	53.80	0.0258
4	7,387	134	53.75	0.0181
5	7,253	98	53.39	0.0135
10	6,886	54	50.10	0.0078
20	6,350	61	42.37	0.0096
30	5,730	61	34.78	0.0106
40	5,109	69	27.16	0.0135
50	4,401	80	19.73	0.0182
60	3,454	114	12.83	0.0330
70	2,161	149	7.27	0.0690
80	750	103	4.10	0.1373
90	92	23	2.29	0.2500
100	1.6	1.6	0.50	1.0000

Compare, CASPER, *Die wahrsch. Lebensdauer*, 1835 ; TOBLER, *Ueber d. Bewegung der Bevölkerung*, 1853 ; QUETELET-RIECKE, *Ueber d. Menschen*, 1838 ; CLESS, *Med. Statist. des Cathar.-Hospitals ;* SZOKALSKI, *Arch. f. phys. Heilkunde*, VI. ; OESTERLEN, *loco cit.*

3. As regards Predisposition to individual diseases, each age is liable to certain diseases, and these diseases run a different course in various periods of life. This is to a great extent explicable by certain anatomical and physiological peculiarities of organs.

The diseases of the fœtus have already been treated of (p. 42). Those affections which cause premature expulsion of the fœtus, so-called abortion or premature labor, cannot be considered in this place.

Compare HEGAR, *Mon.-Schr. f. Geburtsk.*, 1863, XXI.

During labor the child is exposed to pressure upon the head, belly, umbilical cord, and the extremities. Pressure upon the head may produce extravasations of blood upon and within the skull ; that upon the umbilical cord sometimes produces death by asphyxia; that upon the extremities fractures. Even without marked compression, the prolonged stay of the child in the genital passage becomes dangerous, and determines hæmorrhage in the brain, asphyxia, debility, and death. In general the need of breath (*besoin de respirer*) is small immediately after birth, and this explains the often much-prolonged apparent death. Occasionally a too rapid delivery may prove injurious to the child, because it does not in that case feel much need of air, and breathes feebly. Inoculation with gonorrhœal virus while the child is traversing the genital passage (gonorrhœal ophthalmia of the

new-born) is not rare; syphilis, in spite of the *vernix caseosa*, is possible, if there be a wound in the skin, but very rare.

In the course of the first few days after birth, but more especially until the third and fourth days, all children lose weight, and regain their original weight only on the seventh day. The proportional amount of blood is smaller in the newly born than in the adult, being one-thirteenth of the body-weight in the latter, one-nineteenth in the former. The blood has a high specific gravity, contains an abundance of solid ingredients, especially blood-corpuscles, and only little fibrin. The mean pulse-rate during the first week of life is 130 per minute; the blood-pressure is less, and the duration of a blood-circuit shorter in the young than in the grown individual. New-born children inspire forty-four times per minute. During the first hours of life the temperature sinks from 1° to 1.5° C., rising in a few hours to 37.5° or thereabouts, where it remains.

At this time the danger of illness is very great. A kind of revolution occurs in the whole body of the child; various organs enter for the first time into action. Coming from the uniformly warm medium constituted by the amniotic fluid into the air, the organism is made to undergo the most marked acclimation, a more severe one than any which he can afterward experience. If there be any alterations of the heart, of the lungs, or of the nervous system, such as interfere with the respiratory process, they become evident for the first time, and cause death at once, or determine a rapid failure of strength with symptoms of cyanosis, or the so-called atelectasis pulmonum, or produce general debility. The straight tubuli uriniferi frequently contain during the first weeks of life the so-called uric acid plugs; the result in some cases of increased tissue metamorphosis; in others of interruptions in the supply of oxygen during labor; they are never observed in still-born children.

The division of the umbilical cord and the sloughing away of its end frequently are the occasion of local and general disturbances, umbilical haemorrhage, umbilical arteritis and phlebitis, pyaemia, trismus, tetanus. Induration of the skin and subcutaneous connective tissue is a peculiar and severe disease of the nursing age. The so-called icterus neonatorum is produced by the escape of blood-pigment into the tissue of the skin, which is very hyperaemic after birth, and lasts from the middle of the first week to the end of the second. At this age we also, though very rarely, see jaundice resulting from retention of bile, and as a sign of pyaemia.

The predisposition to disease is so strong during the first year of life that one-fourth of all children born die within that period. The greater number of deaths occur in the first month, in the first week, upon the first day after birth. Mortality is greater in those first born than in children born later; it is greater, notably greater, in cities than in the country; greater in industrial manufacturing districts than in agricultural ones; greater among the poor than among those well-to-do; greatest in foundling asylums. During general epidemics the death-rate is the greater in children, as they are attacked sooner after birth. The helpless and dependent state of nurslings seems to have a good deal to do with this great mortality, and in favor of this is the fact that illegitimate children have a much greater death-rate than legitimate ones.

On the average, 9 to 10 per cent. of all children are illegitimate; the larger number in Bavaria and Saxony; the smaller in Sardinia and the Netherlands. In urban and industrial populations the proportion is greater than in the agricultural class (14.7 : 7.6).

A healthy child, male or female, grows in length by more than one-half

its size during the first two years; it increases from 50 cent. to about 79 cent. It trebles or quadruples its weight; that is to say, it weighs 3 to 4 kil. at birth, 10 kil. in the first year, 12 kil. in the second. The following is the rate of monthly increase in the first year, the initial weight being 3.25 kil. : 4.00–4.7–5.3–5.9–6.5–7.00–7.4–7.8–8.2–8.5–8.7–8.9 kil.

Such special determinations of weight increase have not merely a theoretical value, but also a practical one, for by them we can test in a certain manner the usefulness of a given infant-food (mother's milk, nurse's milk, artificial food).

The irruption of the teeth takes place in the following usual order, though deviations are not rarely observed :

From the 5th to the 7th month, the two lower middle incisors.

From the 8th to the 10th month, the two upper middle incisors, and the upper lateral incisors.

From the 12th to the 14th month, the first four molars, and two lower incisors.

From the 18th to 22d month, the four canine teeth.

In the 3d year the second molars.

Children present many peculiarities in organization and mode of reaction which have an influence upon the nature and extent of morbid processes. Most striking is the liability to spasms (reflex spasms). These, in milder forms, such as rolling of the eyes, twitching of the mouth, jerking of single limbs, occur after insignificant provocation in nurslings, as during micturition and defecation. In the various affections accompanied by fever, we also often meet with spasms. This abnormal excitability is attributed to the softness, the humidity, and the rapid growth of the brain. This excitability, however, shows itself only in the motor apparatus; for sensibility is never greater in the young than in the older person; every irritation whose painfulness may be estimated, as flea-bites, itching eruptions, intertrigo, are more easily endured by the infant. Very young children seem to possess a complete immunity to neuralgia. Insanity, with the exception of congenital idiocy, is most rare in childhood. Intermittent fever and typhoid fever do occur, but more seldom than in persons of riper age.

The anatomical peculiarity that the larynx is differently proportioned from that of the adult is of importance. The vocal fissure is narrower, chink-like, the cartilages are softer, and consequently the glottis is more easily closed by spasm. The extreme want of breath and danger of asphyxia, which in the adult can be brought about only by so-called œdema of the glottis, will arise in children without any trace of organic disease (false croup, laryngismus stridulus, asthma Millari). The danger attending true croup is much increased by the narrowness of the air-passages in young children. In the same way the narrow nasal passage of the new-born should be remembered, for because of this coryza becomes a dangerous malady in these subjects, nursing is thereby rendered difficult, and their life is easily brought to a termination by the anæmia of inanition.

Nursing children vomit with the greatest ease. This arises from the position and shape of the stomach; it lies more vertically, and its fundus is but little developed. Disturbances of nutrition, probably of a chemical sort, and diarrhœa are frequent, and cause death by exhaustion. New dangers are encountered when the food is changed or when the child is weaned. The hyperæmia of the mouth, which accompanies the first irruption of the teeth, at times causes hyperæmia of the brain, and convulsions; of less consequence are diarrhœa, and erythema of the skin.

The skin and the mucous membranes are more excitable, more prone to

disorders of circulation. The function of the lymphatics is prominent in childhood, the quantity of lymph is increased, the lymphatic glands have their greatest development; and in the latter we more often observe alterations of nutrition than in adults (so-called scrofulous diseases). Rachitis now begins to show itself, usually in the shape of softening of the occipital bone (craniotabes).

Parasites, especially lice and round worms, readily lodge in these young children; the former because they cannot well clean themselves. The same is true of spores, the cause of thrush; also, perhaps, of ascaris. At any rate, their more frequent appearance in children is evident. Other parasites, such as tape-worm, are rarer.

After the first dentition, severe diseases of the respiratory organs are more frequent, such as pneumonia, croup, tuberculosis of the bronchial glands, whooping-cough.

In the age between one and a half and eight years growth proceeds rapidly, and the cerebral functions are developed. On the average, a child grows in length about 6 cent. each year; the weight of the body goes on increasing to the eighth year, rising in boys to 20 kil., in girls to 19 kil. The blood has a lower specific gravity, coagulates quicker, contains a less amount of solid ingredients, has more red corpuscles. The pulse rate diminishes from 110 to 90 beats per minute in the eighth year; the respiration-rate from 40 to 26. The absorption of oxygen and exhalation of carbonic acid are relatively at a maximum. Hunger and thirst remain pressing (the half-year-old child ingests daily one-sixth of its weight, or even one-fifth, the adult only one-twentieth), and are not as well borne as by adults. Consequently, emaciation during disease is greater. The rapidity and extent of tissue-metamorphosis in childhood are evidenced also in the composition of the urine; a child aged three or five years passes much more in proportion to its weight than a person of about sixteen years; twice or thrice as much urine, with twice or thrice more urea, and more than thrice as much chloride of sodium; the amount of phosphates is, contrarily (because of growth of bones), diminished. The capacity for regeneration is greatest in all tissues (skin, bones, nerves, etc.).

Diseases of the air-passages and of the lung substance are still frequent at this age: among others whooping-cough, tuberculosis of the bronchial glands and lungs. Diseases of the intestines are less as a rule. Danger arises from diseases of the brain, from tubercular meningitis and acute hydrocephalus especially; epilepsy and chorea begin to show themselves. Rachitis, tubercular and simple inflammation of the bones, are the attributes of this age. Constitutional diseases are especially common; we see, in addition to the tuberculosis, scrofula, scarlatina, rubeola, variola. That young children should be particularly liable to the last two of these diseases, does not depend upon a special predisposition in infancy (adults also have these diseases when they have not had them in childhood), but upon the fact that a human being cannot be long in the world without being exposed to infection from both these affections.

From this age until puberty, boys increase 5.5 cent. each year, reaching at the age of twelve years a height of 138 cent., and girls 135 cent., on the average. Boys gain about 2 kil. in weight per year, girls a little more, so that in the twelfth year children of both sexes weigh on the average about 30 kil.

The state of health in this period is, on the whole, favorable. The diseases which do occur in this period exhibit no peculiarities, they are such as have been enumerated. We have now to deal with the morbid

consequences of attendance at school. These so-called school-diseases have their origin in bad ventilation, in bad or at least irregular heating, in too much sitting, in bad body-attitudes. Thence may arise general anæmia and scrofula, superabundance of blood in the head, of congestive or mechanical origin, with headache, nasal hæmorrhage, goitre, scoliosis, usually with convexity to the right, myopia, etc. Besides, attendance at school is important, because of the possible spread of infectious diseases, especially measles, scarlet fever, whooping-cough, diphtheria, the itch, and tinea tonsurans; and because of the acquisition of bad habits (onanism, etc.).

Compare GUILLAUME, *Hygiène scolaire*, 1864. VIRCHOW, *in Archiv*, 1869, XLVI., p. 447.

The period from the thirteenth to the eighteenth and twentieth years is called the PERIOD OF PUBERTY, or development of virility. Youths grow in this period some 30 cent., girls 20 cent. The increase of weight is even more rapid than before, reaching 58 kil. in boys eighteen years old, and in girls of the same age 51 kil. The pulmonary capacity goes on increasing until the twenty-fifth year. The quantity of air inspired is greater than that taken in by adults, so is the expired carbonic acid (even double in some cases), and the expired watery vapor. In this period the mental attributes, exertions, and character take extension, in conjunction with sexual development. The new functions of semen-elaboration, of throwing off of ova and menstruation, afford numerous opportunities for morbid action; in the female sex amenorrhœa, dysmenorrhœa, and chlorosis are frequent, in both sexes there are extravagant notions, disorder of the imagination amounting to positive insanity, this taking the form, usually, of erotic or religious mania. Epilepsy, chorea, hysteria, neuralgia, are by no means uncommon. Sexual aberration (onanism) or sexual excesses often occur, and weaken the body more than they would in later years. The various forms of venereal disease are also frequent in the latter half of this period. All acute diseases occur in this age; among chronic diseases tuberculosis is particularly frequent.

From the twentieth to the twenty-fifth year, until the period of complete growth, the bones and muscles and the thorax especially develop; the thymus gland diminishes in size. The pulmonary (vital) capacity still increases. In the twenty-fifth year the male is 168 cent. in height and weighs 63 kil., the female is 157 cent. high and weighs 53 kil. All severe acute diseases occur in this age. In place of the laryngeal affections noticed at an earlier age, we have more often œdema of the glottis. In females chlorosis is still frequent. Bodily and mental efforts are well endured, and sexual indulgence is permissible if the body be well developed.

MATURE AGE extends in males a year or more beyond forty years, in females almost to forty years: this is the period of highest development. The male attains in the fortieth year his maximum weight, 63.6 kil., and then begins to lose flesh. Women continue to grow heavier (reaching to about 56 kil.) until the fiftieth year. This is the healthiest period, provided that there have not been great exertions, excesses, or ill-health in the preceding youth. At this time gout appears, and with it gastric and hepatic affections, hæmorrhoidal conditions; in women leucorrhœa and other diseases of the sexual organs. Exertions and privations are well borne in this period, and even excesses are not as harmful as in previous years.

The name of CLIMACTERIC AGE, that in which decline begins, is given to the period included between forty-five and sixty in men, and forty to forty-five or fifty in women. Men become more corpulent, women rapidly grow

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older ; in both the size of the body diminishes. Menstruation ceases in
this period, with concomitant disorders, and the development of diseases
of the internal sexual organs and the breasts. Acute diseases are more rare,
but more easily produce death. Abdominal adipose deposit occurs, especi-
ally in men, though without morbid action. Lastly, we find carcinoma in all
organs, prostatic and vesical diseases appear, as well as emphysema and
asthma, and cerebral hæmorrhage.

OLD AGE, at least to the age of seventy, is characterized by diminution of
nutrition ; the so-called *marasmus senilis*. Within this are a number of ana-
tomical and functional alterations ; " *senectus ipsa morbus*." The wasting
of old age consists in diminution of the connective tissue, in atrophy of the
skin and nearly all mucous membranes, as well as of the muscular struc-
tures, even those of the internal organs, gland-ducts, and bloodvessels ; in
gradual diminution of the excitability and energy of the nervous system in
general. The blood exists in smaller amount, is poorer in solids, particu-
larly in blood-corpuscles and albumen. The large bloodvessels are en-
larged because of loss of the elasticity of their middle coat ; many arteries
exhibit deposits upon their inner coat ; a number of capillaries are blocked up.
Through loss of teeth, come numerous alterations of the organs of respira-
tion and digestion, atrophy of blood and lymphatic glands ; digestion, blood-
making, and respiration are impaired ; respiration even more by deposit of
pigment, by atrophy of pulmonary lobules (*emphysema senile*), by sinking
in of the vertebræ, and by ossification of the costal cartilages. The respir-
atory movements are more frequent but more shallow. The absorption of
oxygen and exhalation of carbonic acid are less in aged persons. The
amount of urine, as well as of its solid ingredients, is diminished. The
body temperature, strange to say, is a little higher than in adult age. The
absolute amount of heat, however, is less, and so is the power of resisting
cold. The brain undergoes a marked degree of atrophy, the resulting space
being filled up in part by thickening of the meninges, in part by accumula-
tion of serum in the ventricles ; yet the senile brain dropsy is not the essen-
tial attribute of this period of life ; there are usually observed only stubborn-
ness and imbecility in certain lines of thought. The bones become more
fragile in consequence of increase in their medullary substance.

All the above are in a measure normal events, and the aged seldom die
of them. Almost always there are found in the body well-developed new
anatomical lesions, which have, however, given rise to but ill-defined
symptoms during life. To this category belong many vascular and cerebral
diseases, pneumonias, cancer in various organs. Nearly all chronic affections
are still common ; among acute ones, typhoid fever very seldom occurs, the
acute exanthemata not at all. (*Vide infra*, senile marasmus.)

3. SEX.

Compare the literature of diseases of trades by RAMAZZINI, 1700 ; PATISSIER,
1822 ; VILLERMÉ, 1840 ; FUCHS, CASPER, CLESS, HALFORT, 1845 ; BROCKMANN,
1851 ; etc. The literature of female diseases by OSIANDER, 1820 ; SIEBOLD, 1821 ;
JÖRG, 1831 ; MENDE, 1831-6 ; LEE, 1853 ; COLOMBAT, 1838 ; FRÄNKEL, 1839 ;
BUSCH, 1839-44 ; MEISSNER, 1842 ; MOSER, 1843 ; KIWISCH, 1847, 3d ed. in 1851 ;
GRAHAM, 1850 ; JONAS, 1850 : SCANZONI, 1862 ; VEIT, 1867 ; THOMAS, 1874. The
literature of midwifery.

The influence of sexual difference upon disease arises from the original
and physiological differences between man and woman. In the latter there
being less toughness and density of all the tissues ; less development of
the bones, of the striated and smooth muscles, of the external skin, and per-
haps also of mucous membranes ; lesser size of the digestive apparatus and

the great glands, as well as of the kidneys ; positively as well as relatively less tissue metamorphosis ; smaller need of food ; less development of the respiratory apparatus ; smaller vital capacity of the lungs ; smaller formation of carbonic acid ; less perspiration ; a smaller amount of blood, particularly of blood-corpuscles as well as of fibrin, a greater proportion of water, salts, and albumen ; smaller volume and weight of the brain ; greater fatty deposit, etc.

Again, the two sexes show different results in consequence of differences in mode of life and education. It is sufficient to remember that men are more subject to all those diseases which are especially or solely caused by unfavorable hygienic conditions, or which are of meteorological origin, such as pneumonia, pulmonary emphysema, heart-disease, and articular rheumatism ; and to such affections as are caused by occupations and professions ; and lastly to recall the efficacy of such causes of disease as the abuse of alcohol and tobacco.

On the contrary, women find more often exciting causes of disease in education and customs. Nervous irritability, hysteria, and spinal irritation have their origin in the absence of practical activity after which follows healthy fatigue, in actual immersion in the contemplation of the state of one's body, in excitation of the sexual appetite without opportunity for its gratification ; women of the higher classes are especially liable to these diseases. The preponderance of this morbid group in women is so very great that the above causal conditions are not sufficient to account for the disproportion : and this is particularly true of hysterical spasms of all kinds, which are very seldom met with in men. In this question there probably enters some yet unknown peculiarity in organization.

Those affections of the brain, spinal cord, and nerves, which are more especially produced by directly acting morbid influences, are not more frequent among women than men. As regards insanity, the statistics of various countries show an excess sometimes of males sometimes of females ; the latter is the case where women take more part in the occupations, cares, and emotions of men, as in France. In the male sex almost the only spasmodic affections observed are epilepsy and tetanus ; among women epilepsy is not as frequent, tetanus is very rare. On the contrary, reflex spasms of all kinds are very common in women. Paralyses are, in comparison with females, very frequent in males. Diabetes mellitus, gout, locomotor ataxia are very much more common in men than in women. That vesical diseases and vesical calculi should be more common among men may be accounted for by the structure of the urinary organs. Women seldom suffer from hæmorrhoids, which fact may possibly be connected with the periodic loss of blood at menstrual periods ; yet they, contrarily, often have struma.

The greater frequency of disease in female fœtuses is as yet of unknown causation. OTTO found that among 473 cases of malformation in which the sex could be determined, there were 270 females and 203 males. On the contrary, the so-called transposition of organs is much more common in men than in women.

In all countries there are more boys born than girls (in the proportion of 105–106 to 100) ; the number of boys still-born is greater than that of girls (14 : 10). This last circumstance is probably due to the fact that on the average the body of the mature male fœtus is larger and heavier than that of the female fœtus, and that, consequently, there are greater impediments to the birth of boys. Greater mortality prevails among boys after birth, so that if we reckon one-year-old children the preponderance of males is quite obliterated. This proportion continues throughout life, so that

almost without exception women outnumber men (102.7 : 100). From the second year to puberty there are no marked differences in the diseases of the two sexes, except that boys are more liable to laryngeal croup, and that later on girls are more often the subjects of chorea. During the period of puberty the female sex exhibits more affections of the sexual organs than males. This is explicable partly by their greater size, different location, especially reduplications of peritoneum, partly by their more complicated structure, and partly by their irregular performance of function. Anæmia of development (chlorosis) is especially the attribute of the female sex. During youth both sexes share acute diseases about equally; among men pulmonary and pleural inflammations are more usual, in women those of the peritoneum a little more frequent. Those dangers to which women are exposed during pregnancy, confinement, and lying in, by affections of the sexual organs and the breasts, are counterbalanced in men by bodily and mental strains, to which they are exposed in their occupations. Among chronic diseases those of the digestive organs, such as colic, ulcer of the stomach, constipation, as well as diseases of veins, are more common in the female sex. Those diseases which absolutely cause the greatest mortality, such as tuberculosis and cancer, are about equally divided between the two sexes.

In all diseases women endure better than men. Severe pain, great loss of blood, continued ill-health, exhaust men quicker than women. As regards their relations with physicians, women, aside from the insufferable pranks of hysterical ones, are more patient, tractable, and thankful than men.

The mortality ratio of both sexes is indicated in the following table of QUE-TELET.

Out of 10,000 individuals there survive—

AT THE END OF	IN CITIES.		IN THE COUNTRY.	
	MALES.	FEMALES.	MALES.	FEMALES.
1 month	8,840	9,129	8,926	9,209
2 months	8,550	8,916	8,664	8,988
3 "	8,361	8,760	8,470	8,829
4 "	8,195	8,641	8,314	8,694
5 "	8,069	8,540	8,187	8,587
6 "	7,961	8,473	8,078	8,490
1 year	7,426	7,932	7,575	8,001
2 years	6,626	7,179	6,920	7,326
3 "	6,194	6,761	6,537	6,931
4 "	5,911	6,477	6,326	6,691
5 "	5,738	6,295	6,169	6,528
6 "	5,621	6,176	6,038	6,395
8 "	5,481	6,026	5,862	6,215
10 "	5,384	5,916	5,734	6,082
15 "	5,241	5,732	5,502	5,796
20 "	5,038	5,500	5,242	5,484
30 "	4,335	4,881	4,572	4,812
40 "	3,744	4,208	4,134	4,112
50 "	3,115	3,592	3,588	3,458
55 "	2,739	3,225	3,194	3,118
60 "	2,329	2,862	2,767	2,762
65 "	1,859	2,397	2,277	2,310
70 "	1,372	1,864	1,713	1,758
75 "	891	1,261	1,114	1,182
80 "	463	682	566	619
85 "	184	289	239	262
90 "	49	86	67	71
95 "	9	18	14	18
100 "	0	1	1	1

4. CONSTITUTION—HABIT—TEMPERAMENT.

By CONSTITUTION is meant a sort of physiological basis, a predisposition, presenting itself as something constant in the same individual, and characterized by the mode of reaction of nerves and muscles, and also by the composition of the blood and by nutrition, as well as by the power of resistance to external and internal influences. These conditions sometimes persist without change during the individual's whole life, and sometimes are altered by change of conditions of life (nutrition, dwelling, calling, etc.), or by diseases. By HABITUS (habit) we understand the external expression of the constitution; these are related, as are the group of symptoms to internal conditions of disease. The term TEMPERAMENT is applied to something special in the constitution, as, for example, the humor, or frame of·mind, and the mode of manifestation of the activity of the brain.

The various forms of constitution lie in part in the domain of healthy life, and in part correspond to morbid states, or shade into morbid constitutions. They are as little derived from nature, and as little defined as are forms of disease. There are as many constitutions as human beings, just as there are as many diseases as sick people. But, as we set up certain definite forms of disease for the sake of description, so we pick out the most distinct types of constitution.

1. THE STRONG OR ROBUST CONSTITUTION. The body is larger, or of medium size, broadly built, the skeleton and muscles are strongly formed; the pulse is full, calm, and not variable, the blood rich in blood-corpuscles, there are rare, deep, respiratory movements, with great vital capacity, abundant perspiration, concentrated urine, good digestion and nutrition; the functions of the brain are not too much developed. This constitution is seldom met with in women, never in youths, only in men between twenty and fifty years of age, most frequently in those classes who enjoy good food, together with physical exercise.

Some would separate from the above the PLETHORIC CONSTITUTION; characterized by a more compact, broader build, abundant muscular substance, red cheeks, lips, and mucous membranes; sudden movements, sometimes a short neck.

As attributes of this constitution are favorable conditions of health; great power of resistance to the action of external and internal influences; rapid recuperation; frequent acute diseases: pneumonia, rheumatism, typhoid fever; among chronic diseases: cardiac diseases, gout, pulmonary emphysema; tuberculosis only when there is an hereditary taint.

2. THE IRRITABLE CONSTITUTION, the most common, especially in women and children.

The characters of this constitution are, small muscular development, a pale and not over well nourished skin, marked development of the intellectual faculties, lively temperament.

The following subdivisions may be made. The CONSTITUTION WITH CEREBRAL IRRITABILITY, as exists in such individuals as easily become delirious in fever; that with SPINAL IRRITABILITY, as in those who easily have convulsions; the CATARRHAL CONSTITUTION, in which there is a dry, easily moistened, or flabby skin, with evident tendency to catarrhal inflammation; the WEAK-ANÆMIC CONSTITUTION, with pale skin and mucous membranes, small muscles, exhaustion quickly induced. The BILIOUS CONSTITUTION might be added to this list, a frequent one in southern countries, showing a dark or yellow skin, dark irides, a lively and often suffering glance.

3. THE INDOLENT CONSTITUTION: Marked by slow development, slow and not abundant movements, ease of fatigue; the bones, fat, and glands more developed than the muscles and nerves. The skin is lustreless and stiff; recovery is slow. As subdivisions we have the venous, lymphatic, asthenic, and cretinoid constitutions.

It is to a very great extent an error to assume that the various constitutions predispose to certain diseases. There are differences as regard the course of disease, the absorption of exudations for example, which is slower in the indolent constitution. For therapeutics the matter is also of a certain importance, since, for example, individuals of indolent constitution, and many of the irritable constitution, do not well bear bloodletting, and, in general, any debilitating means or methods.

The HABIT is made up of the size and weight of the body, its degree of fatness; also in part of the form and color of external parts, the bearing of the body, the turgescence of organs.

It is only with regard to size and weight of the body in man, and in some few animals, that several important physiological and pathological characteristics are known. The extreme body-weights in proportionately grown adults are as $1 : 2\frac{1}{2}-3$; those of height are as $1 : 1\frac{1}{3}-1\frac{2}{3}$. The pulse is slower in large men then in small men of the same age, or in other words, the length of the pulse-beat increases with the body-length. The time required for the completion of circulation increases (in animals) with the weight and length of the individual. Grown persons of short stature have a much greater amount of blood relatively to their body-weight than tall individuals. Large men have larger lungs, a larger larynx, etc. The vital capacity increases in men at the rate of about 60 C. cent. for each 1 cent. in height. Small men breathe oftener, though less deeply, than large ones. The relative (to body-weight) amount of the products of respiration is larger in small men than in tall ones. The absolute tissue-metamorphosis is greater in tall and heavy persons, while their relative amount is in just reversed proportion. With respect to the deposit of fat there are also certain data worth remembering. Lean individuals have on the average a greater appetite, and absolutely and relatively (to body-weight) more intense tissue-changes than fat persons. The latter have relatively less blood; they consume less oxygen, and have a smaller pulmonary vital capacity; they secrete less bile, much less lymphatic fluid, and but little urine.

The influence of these various forms of habit upon disease in general, upon its course, treatment, etc., cannot be briefly related. We know that fat, though otherwise healthy persons, resist but feebly many morbid internal and external influences, that they are more often the subject of many forms of cardiac, hepatic, and renal disease, and that they do not well bear energetic therapeutic interference.

Compare VIERORDT, *Grundriss d. Physiologie d. Menschen*, 1871, p. 553.

Besides the use of the word habit in the sense above defined, the term is often applied to marked alterations of the constitution, or to the external evidences of latent morbid action. Thus we speak of the phthisical habit, the carcinomatous and apoplectic habits, etc., without meaning to say that phthisis or cancer is actually present.

With respect to TEMPERAMENT, great efforts have been made to connect its various types with given diseases. But the conception of a temperament is very vague, and as soon as the physician attempts to bring it out in its material manifestations, it fades into the definition of constitution.

From a very ancient period the division into PHLEGMATIC, CHOLERIC, SANGUINE, and MELANCHOLIC temperaments is recognized. The originals of these are met with,

as well as those of several other types which have been defined in more recent times. In the quiet or phlegmatic temperament there are a flabby state of the muscular system during repose, want of energy in the involuntary muscles, turgescence of the tissue, a disposition to adipose deposit, small or slow reaction to psychic excitation, slightly developed passions, small sensibility to bodily suffering. In the choleric temperament we find active contractions of the voluntary muscles, producing a tense, firm habit of body, great irritability, with force and persistence of the irritation, strong passions. The sanguine temperament is characterized by marked irritability, and equally great liability of the nervous system to exhaustion, sudden changes in the activity of the special senses and in humor, these changes being produced by bodily exertions as well as after mental exertion and emotional excitement. In the melancholic or sentimental temperament there are found united slight irritability with strong capacity for reacting to sensory excitations, and great persistence of the frame of mind, especially that of dulness or sullenness.

It is possible that difference of temperament may have a certain influence upon the origin and course of diseases, especially the psychical; no such influence has been demonstrated as affecting somatic diseases.

Whether the COMPLEXION (brunette or blonde) can affect disease is not known. The notion that blonde women suffer more from leucorrhœa is a mere popular prejudice. On the contrary, it would seem that cancer of the uterus is more frequent in brunettes.

With respect to RACE, the extreme susceptibility of negroes to disease has always been maintained. In general this question is complicated by the interference of climatic and hygienic causes.

II. EXTERNAL CAUSES.

1. ATMOSPHERIC INFLUENCES.

A. ATMOSPHERIC PRESSURE. Atmospheric pressure is a tangible phenomenon, yet one which it is difficult to appreciate in its influence upon the body, because it seldom acts alone. There are two important factors united in atmospheric pressure changes; the quantity of oxygen in the air diminishes in equal volumes with the rarefaction of air, the loss of perspirable material increases with the rarefaction.

The effects of increased atmospheric pressure have long been known to divers; in more recent times these have been more accurately studied during the building of bridges by the pneumatic method, and in institutions where compressed air has been put to therapeutical uses (the so-called baths in compressed air—pneumatic institutions). In these conditions there occurs a momentary disturbance of the equilibrium of gases in the cavities in the transition from a lighter to a denser air. This is made most frequently and most painfully evident in the air by a depression of the tympanum. Movements of deglutition which open the Eustachian tubes, as well as attempted expiration with closed mouth and nose (Valsalva's experiment so called) equalize the atmospheric pressure on both sides of the tympanum. Severe and in part dangerous manifestations attend very sudden diminution of high atmospheric pressure, effects probably explicable by the increase of blood-pressure and by the formation of embolic stoppages in vascular areas by air which has suddenly been set free from the blood and has mingled with the circulation. These are nervous pains, hyperæsthesia, muscular weakness, sometimes convulsions, etc.

Similar phenomena appear in unnaturally dense air, as in breathing air too rich in oxygen. With respiratory movements of equal extent in such air there occurs a greater degree of oxidation and carbon-excretion than

while breathing under usual atmospheric pressure. There can be no question, probably, as to the after-effects of a stay in such air upon the chemistry of the respiration. Breathing in a pneumatic apparatus unconsciously and involuntarily is done with more distended lungs than under ordinary air pressure, and this (the lowered position of the diaphragm) is to be explained by the compression of the intestinal gases. The respiratory movements are deeper and less rapid (sometimes reduced one-half). The arterial blood-pressure decreases; the pulse becomes fuller and usually slower; the capillaries are contracted; the temperature rises. The cutaneous and pulmonary exhalations are diminished, the urinary secretion is increased according to some authorities, decreased according to others; the appetite is greater; the body-weight increases. The subjective sensations experienced during a long-continued stay in compressed air are described as nearly always agreeable. Muscular movements are more easily performed; speech is impeded; dyspnœa is often subdued.

Compare VIVENOT, *Zur Kenntn. d. physiol. Wirk. u. d. therap. Anwend. d. verdicht. Luft.* 1868. PANUM (*Arch. der Physiol.*, 1868, 1, 2, u. 3 H). A. H. SMITH, *Effects of High Atmosph. Pressure*, Brooklyn, 1873, and others.

The effects of diminished atmospheric pressure have been observed on a large scale at high elevations; although there are superadded the influence of cold and of various efforts which must affect the result. Experience in the Alps, the Himalayas, and especially in the Andes of South America agree in that healthy persons feel nothing unnatural at a height of 5,000 to 7,000 feet. It is only when an elevation of 9,000 to 18,000 feet, where the atmosphere is one half lighter, is reached, that shortness of breath, acceleration of the pulse, rapid exhaustion, and a remarkable immunity to the effects of alcohol are observed; these together with weakness, headache, syncope, bleeding from the gums, nose, etc.

New-comers upon those elevated parts of the Andes suffer from "*puna*," or "*sorocho*," an acclimation disease, characterized by piercing chilliness, headache, and nausea.

The same symptoms are observed in those who go up in balloons.

Some individuals resist the effects of rarefaction of the atmosphere. The aeronauts Green and Bush ascended to an elevation of 27,000 feet, with a barometer standing at 10. 32″; the first 11,000 feet having been traversed in seven minutes. Yet they experienced neither acceleration of the pulse nor quickened respiration, not even when they exerted themselves in throwing out ballast. GLAISHER attained a height of 33,000 feet.

The redness and swelling of the skin, the occasional hæmorrhages from the skin and from exposed mucous membranes, are easy of explanation. The same is true of the early outward bulging of the tympanum, with ear-ache and hardness of hearing. The chapping and cracking of the skin, and the consequent ulcerations, are dependent upon the co-existent dryness of the air. The loss of turgescence in the lineaments of the face, the diminution of perspiratory and urinary secretions, and the increase of thirst may be also referred to the same cause. The drowsiness, headache, and vertigo are probably owing to cerebral anæmia. The weakness is in part explained by the diminished firmness in the fixation of heads of bones in their sockets, particularly at the shoulder-joint, as well as by the rarefaction of the intestinal gases which impinge upon the diaphragm; the shortness and quickness of breathing by the complete distention of the lungs; the increase of the heart's action by the removal of pressure from the bloodvessels.

Under these circumstances contradictory phenomena show themselves in the sick. One would suppose that the release of the thorax (from the usual pressure) would operate favorably upon the pulmonary circulation, making it more active, and that, consequently, tubercular patients would derive benefit from a residence in high localities. This is indeed what occurs in many cases, independently of the fact that tuberculosis does not occur upon high mountains. Then we have the experience with compressed air, which used in unusually heavy amounts (2–3 atmospheres) has done good to many having dyspnœa; and which when employed systematically has much improved emphysematous and tuberculous lungs.

If, now, the most extreme rarefaction of the atmosphere has little or no effect upon some persons, if a diminution of several inches of pressure is well borne by mountain travellers, it is not permissible to conclude that variations in atmospheric pressure, occurring in one locality and amounting to a few lines or one and a half inches of mercury in rise or fall, can have any important effect upon healthy persons. It may be said that it is not so much extreme changes, as permanently high or low barometric pressure, which gives a particular stamp to the epidemic constitution; and yet man becomes very easily acclimatized in the high regions. Perhaps it is only the frequency of variations which is injurious.

The scanty empirical statistical investigations on this point have yielded results of doubtful value. According to CASPER, mortality increases with the atmospheric pressure. This is true only in Berlin, or at all events Dresden, and a few years in Paris, but not at all in Hamburg, where a high barometric pressure is more favorable to life than a low one. It would seem that consumptives die in notably smaller number in Berlin during high barometric pressure than during a low one. In New York (observations extending over three years) it appears that pulmonary and uterine hæmorrhages usually coincide with a falling barometer (GOSLIN, in *Canst. Jahresb.*, 1843, p. 186).

We are enabled to observe the effects of diminished pressure upon limited parts of the body during the application of a cup. Under it blood accumulates, and in consequence of relatively increased pressure round about, exudations and extravasations take place. Naturally we cannot conclude from these alterations of equilibrium as to the consequences of generally diminished atmospheric pressure, because the pressure is rapidly equalized in all the open cavities of the body, and the possible variations are not very great and sudden.

B. THE TEMPERATURE. The effects of temperature upon the organism are either local, or general. The results vary according to the kind of temperature (heat or cold), according to the duration of its action, and according to the variations (so-called chilling) of temperature. In the medium temperatures the degree of inuring is of importance.

(a.) THE LOCAL EFFECTS OF TEMPERATURE. The various extremes of heat and cold which affect certain parts of the body, especially the external skin and the mucous membranes, cause various disorders of circulation, particularly anæmia and hyperæmia, later different forms and degrees of inflammation, and at last (the so-called highest grade of burning and freezing) gangrene (compare this process). After extensive burns of the skin the temperature of the body sinks by several degrees, and does so because lessened elasticity of the arteries produces a dilatation of bloodvessels and increased radiation. Another consequence of this dilatation is diminution of blood-pressure. These phenomena are frequently followed by death. Correspondingly large congelations of the skin do not come under our observation.

WERTHEIM (*Wochenbl. d. Gesell. d. Wiener Aerzte*, 1868, No. 13) observed in cases
of burns made upon the chest and abdominal walls of dogs by means of often repeat-
ed scorchings with turpentine, a constant, definite anatomical change in the blood.
Venous blood drawn from the animal a few minutes after the burning showed,
besides the normal constituents, a very large number of rounded bodies measuring
.001 to .004 mm., having very much the appearance of round blood-corpuscles. Their
number is sometimes as great as, and even greater than is that of the normal red cor-
puscles, and the larger the more severe the burning, but they are always more nu-
merous than in normal blood :—he also saw numerous red corpuscles, apparently in the
act of segmentation, and from which the above described corpuscles had most likely
derived,—many white cells (leucocytes) whose number was not rarely equal to that of
the red corpuscles. And this experimenter had already discovered after burns that
the temperature of the subcutaneous connective tissue just under the part burned
reached 50–70 C. immediately after the greatest burning, and he also constantly
found melanine in molecular and flaky states along the capillary vessels in the focus
of injury :—and, lastly, he always made out Bright's disease of the kidneys after
death.

The cause of death after extensive burns is, according to many authorities, rapid
inanition ; according to others, collapse (shock), etc. ; according to FALK (*Virchow's
Archiv*, 1871, Bd. LIII. p. 27), it consists in paralysis of the heart, which is itself
the result of suspended tonus of bloodvessels.

The effects of different temperatures upon cells, such as it may be observed in
living animals, and by the use of the microscope and heating apparatus (the so-called
moist chamber), will be studied farther on. In an increased temperature nerves and
muscles exhibit an increase in irritability and contractility, although farther on (at
49–50 C. in man) this is followed by loss of vitality. Blood-corpuscles, glandular
cells, etc., suffer in the same way.

β. THE GENERAL EFFECTS OF TEMPERATURE. When there is prolonged
exposure to a low temperature, such as precedes death by freezing (in our
own regions, but especially during voyages in the arctic countries), there
are noted diminution of the desire and possibility of moving, followed by
inability to move, dulness of the senses and the intellect, stupidity, irre-
sistible inclination to sleep, unconsciousness, and actual death. The imme-
diate cause of all these phenomena is probably anæmia of the brain.

WALTHER (*Virchow's Archiv*, XXV., p. 414; *Berlin. Centralblatt*, 1864, No. 51,
and 1865, No. 25) has performed experiments upon the influence of cold, placing the
animals in a tin box, which they completely filled, and which box was wholly sur-
rounded by a freezing mixture of ice and salt—the head of the animal being allowed
to project through a small opening in the box. An animal, cooled to 18 or 20 C.,
and then placed in a medium of the same degree of heat as that proper to the animal,
was not able to recover its normal temperature (BERNARD, *Leçons*, etc., 1856). If
the animal was exposed in a slightly colder medium, as, for example, to ordinary air
temperature, it became cooler and cooler, and ultimately died. If the animal was
taken out of the tin box it was unable to stand upon its feet, but lay motionless upon
its side. Nevertheless, voluntary motion, reflex movements, and sensibility per-
sisted. The heart-beats became very few—reduced to 18–20 per minute. The respi-
ration wholly ceased, or became very rapid, though imperfect. All the excretions
were suspended, especially the urinary. The creature's eyes remained widely open.
A definite degree of animal heat, at which the functions of the nervous and muscular
systems ceased, could not be made out ; death taking place under various circum-
stances at different degrees of body-heat. Animals which died or were killed during
the process of refrigeration, exhibited a constant hyperæmia of the lungs, with serous
exudation in the parenchyma and bronchi. In white rabbits, which died by freezing,
Walther saw the fundus of the eye become quite pale just before death ; then fol-
lowed convulsions and death. The author explains this phenomenon by anæmia of
the nervous centres consequent upon the diminished heart's action. Refrigerated
animals may be restored to the normal degree of heat by artificial heating to 39 C. ;
by artificial respiration, only when, however, the temperature of the surrounding air
is not more than 2 or 3 C. lower than the normal heat of the animal. The means
by which the organism is overcome in the conflict with approaching refrigeration
(heat-inanition) are, contraction of the tissues and capillaries in the superficial parts
of the body, and by the diminution of the frequency of cardiac contractions.

During the prolonged action of an elevated temperature, the skin first becomes warm, moist, and later covered with a profuse sweat; the respirations become quicker, the pulse is smaller and accelerated. Later the subjective feeling of heat becomes more and more severe and more disagreeable, the skin becomes dry, and headache supervenes. With peculiar symptoms death then ensues (sun-stroke or heat-stroke, so called).

According to FORDYSE, BLAGDEN, and others, the following symptoms have been observed in men exposed to a temperature of 100° C. and over : the skin is much reddened, the perspiration is increased, the pulse becomes more frequent, and the temperature itself rises by 1 or 2 (some 2° or 3°, if the air is overcharged with watery vapor, as in the Russian bath). The exposure cannot be prolonged beyond ten or fifteen minutes.

OBERNIER (in his work entitled *Der Hitzschlag,* 1867) has made an experimental study of the effects of high temperatures (40 C.). Animals who remain a long time exposed to a temperature a few degrees higher than their own body-heat, experience a rapid increase of body temperature ; this being caused by the interference of a circumambient high temperature with radiation of heat from the body. This radiation ceases the moment that the temperature of the air equals that of the body. In such a temperature 77 per cent. of the increased heat (in man) is retained in the body, unless certain regulators of body-heat show increased function. This moderation of increased heat is brought about by perspiration and increased evaporation in the heated external air ; by quickened respiratory movements and the resulting loss of water ; by heating of the blood and bloodvessels ; by increased micturition. The body-heat is notably raised by movements, especially when the air temperature is nearly equal to or excels the body-heat. The rapidity of evaporation diminishes with the greater dampness of the air, more particularly in a calm. The animals exhibit very much increased respiratory and cardiac action. If their body heat reach 44 C. there usually appear strong convulsions. After these the animals are unconscious, their respirations are deep and few, the pulse hardly perceptible, the mucous membranes cyanosed. They die with a rapidly increasing body-heat (up to 45 C.) and convulsions, if they receive neither food nor drink in from two to four hours. The heart is in a paretic state even before death. After death the right side of the heart is found distended with blood, the lungs and brain show passive congestion.

WALTHER (*Med. Centralblatt,* 1867, No. 49) has experimentally investigated the action of radiating heat upon the animal frame. He found that rabbits and dogs were killed in one or two hours by the direct heat of the sun in an atmospheric temperature of 21–31° C. During this period the heat of the animals (measured in the rectum) measured 44 to 46 C. The animals thus exposed died cyanosed, with extremely rapid respirations and heart-beats, with tetanus and dilatation of the pupil. The muscles were rendered turbid, appeared distinctly striated in the longitudinal and transverse directions, as after boiling.

The *post mortem* changes observed by OBERNIER are substantially the same as have been seen in human beings who had died of sun-stroke. (Compare *Schmidt's Jahrb.*, CXXIX., p. 292.)

The general influence of extremes of heat and cold, as they occur in our temperate climate, is not unfavorable to the performance of all functions, because the organism quickly and easily accommodates itself to the various not excessive changes of temperature. The large loss of heat in winter causes increased heat production, and the less deperdition of heat in summer causes a diminution of body-heat; both so corresponding that an almost uniform temperature is the result. During exposure to cold, the low temperature and the diminished cutaneous circulation diminish the radiation of body-heat, and the perspiration, thus preventing the cooling by evaporation. During exposure to heat the evaporation of the much-increased perspiratory secretion is a most important refrigerating agent. With increasing cold, the number and depth of the respiratory movements, the carbonic acid of the expired air, the volume of inspired air, and the absolute quantity of carbonic acid, probably also the aqueous

vapor, as well as the absorption of oxygen, are increased. The absolute amount of fixed urinary ingredients is augmented. These results render possible the bearing of extreme degrees of heat and cold, especially when those parts which are most exposed to heat (the head), and those which suffer most from radiation in the cold (extremities, nose, ears), can be protected. Under such circumstances the limits of temperature compatible with human existence are pretty large. An atmospheric temperature of from $+12°$ to $32°$ C. is that best endured by the human body. It may, however, support a heat of $+50°$ C. (which is felt in hot countries only in the sun), and a cold of $-46°$ C. (which may be met with in Siberia). In order to support life at these extreme temperatures it is necessary that the body should have the benefit of all natural aids: in order to resist cold one must be warmly clad, keep up active movements, and eat nutritious food ; in hot weather one must drink a good deal in order to obtain cooling by the evaporation of the perspiration, and keep quiet.

Atmospheric temperatures which equal or surpass the normal body heat (37 C.) become difficult to bear, because our skin is accustomed to feel a cooler surface on the outside than on the inside. Habit here does a great deal : in summer a temperature of 25 C. is delightful, while in winter it would appear unendurable. A few degrees of heat (10 to 15 C.) are very agreeable in winter, yet at such a temperature in summer we should complain of being cold, even if we were warmly clad.

Endurable temperatures may derange health in two ways : either by their uniform long continuance, or by sudden variations.

What may be said of the results of long-continued, uniform, extreme temperatures, is based upon the comparative statistics of diseases, or merely of the deaths, studied in years or in climates in which high or low temperatures have prevailed. The general result, as concerns death-rate, is that the greatest mortality occurs in the coldest months, and the least mortality in the warmest months. March and April are the months in which we find the greatest number of deaths in the climates which have been studied. A large proportion of these deaths are not caused by diseases which have developed in these months, and which consequently were influenced by temperature, but by older affections, which have gone on to a fatal termination under the influence of temperature, and more by its variations than by its absolute degree.

It is interesting and even more important to attempt to ascertain the number and nature of morbid states which arise under varying conditions of temperature. The results of such an inquiry are different in various localities, but nowhere do we obtain a maximum in winter. The majority of diseases occur either in the spring, or in the summer, or are equally divided between each. As regards the nature of disease, we can say with accuracy that the respiratory organs suffer more in winter and spring than in summer, and in tropical countries the digestive organs and the glands (the liver) are more commonly affected. We may also say that brain affections in general, and tetanus, are more frequent in the summer ; sudden deaths and apoplexy are more often seen in winter and spring than in summer and autumn. As regards epidemics, cholera and dysentery are more common in summer ; scarlet fever, measles, small-pox most frequent in winter and spring ; typhoid fever appears most often in summer, fall, and winter, seldom in the spring ; in our countries intermittent fever appears only in spring and autumn. Still, in epidemic and endemic diseases the temperature of the air is not the only causal influence, as is best seen in the case of the plague.

The organism suffers more often and more severely by sudden changes of temperature than by a long continuation of an extreme degree of heat or cold, and even by the contrast of temperatures which by themselves are perfectly bearable and have been often borne without evil result. This phenomenon is called "catching cold," or refrigeration. This operates to the most marked detriment of health, if the differently heated air is in rapid motion (draught), and if it strike against a portion of skin which was previously covered, or which is actually perspiring.

With this understanding, "catching cold" may be designated as an ætiological fact. Of the truth of this every one, even the most incredulous, may become convinced. But this ætiology is often misapplied by lay people, and by some physicians referred to thoughtlessly, and the phenomena remain shrouded in much darkness.

Many healthy and sick persons doubtless expose themselves day after day to changes of temperature, and yet experience no evil results. If the temperature of a room be $+15°$ and that of the outside air $-15°$, we obtain a difference of $30°$, and yet fewer people catch cold in the depth of winter than in spring and summer, when the difference is of a few degrees. In cold weather we take particular pains to protect ourselves, and people of a northern climate are much more careful in this respect than those of southern countries, or even than the inhabitants of central Germany. If we expose ourselves daily to such changes of temperature, we cannot determine with accuracy whether a disease which appears in us is connected with a refrigeration. When the disease has made its appearance it becomes very easy for every one to remember having "caught cold." These considerations are not, however, sufficient to deny the possibility of the sequence. Two phenomena testify to the association of a disease and refrigeration : either the person refrigerated feels disagreeably at the time of catching cold, soon becomes chilly ; or, secondly, there soon follow general morbid sensations, and the beginning of decided symptoms of disease. This occurs so often that we are authorized to assume a relation between the refrigeration and the disease.

The diseases which certainly arise in this way, are particularly the so-called rheumatic affections ; that is to say, those morbid states of the joints and muscles attended by wandering pains, as well as catarrh of the mucous membranes—of the nose, larynx, bronchi, of the intestines, particularly of the large intestines. More doubtful is the connection between refrigeration and the more severe endemic and epidemic diseases, concerning which we know that they certainly develop without refrigeration. Still it cannot be denied that in cholera-seasons refrigeration may be the proximate cause of an attack of cholera ; and that after chilling, an intermittent fever will show itself after the individual has long been removed from the influence of the miasm.

Another point is the relation of the chilled surface to the organs lying near. Refrigeration of the neck causes, it is well known, catarrh of the larynx, that of the chest, bronchitis ; a cold in the head is easily produced by passing from a warm room into the cold air (and *vice versa*) ; disorders of menstruation are produced by chilling of the feet ; diarrhœa very often is set up by refrigeration of the skin of the abdomen. But then we also meet with another result, viz., that if an individual has a so-called tender part (*pars minoris resistentiæ*), that part becomes diseased, no matter where the chilling may have acted.

We have no further positive knowledge of the doctrines of refrigeration (catching cold). The notions which have been advanced concerning the

connection between refrigeration and the diseases which arise from it, are separable into three theories. In the first place, it is claimed that the cutaneous secretion is arrested by the chilling, that consequently injurious substances are retained in the blood, and that the local diseases which follow upon the chilling depend upon the deposit of these substances. All three elements upon which the theory rests are pure fictions. (1.) It is by no means certain that the exhalation of liquid from the skin can be materially deranged by chilling: (2.) no one has ever seen the poisonous material which is said to be retained in the blood: and (3.) it has never been discovered in the diseased part.

Above all, the phenomena which occur after a complete arrest of the perspiration by varnishing or lacquering of the skin of animals deprived of feathers or hair in nowise resemble those which ensue after catching cold. A second view seeks for an explanation of the morbid state by supposing a transient suppression of the cutaneous secretion and its reaction upon tissue metamorphosis, causing in a measure a mechanical reflux of the animal liquids. A third theory refers to an affection of the nerves of the chilled skin, and to their connection with the nerves of other organs. The activity of the skin exhibits itself in the excretion of sebaceous matter, and of water with constituents held in solution, which latter appears in the forms of sweat or of vapor as insensible perspiration. Because of its purely local relations, and of its incapacity for evaporation, the sebaceous matter may be left out of consideration. The aqueous excretion varies extremely, according to the degree of external temperature and the amount of corporeal activity. A draught of air, however, which strikes upon a moist surface, must produce a much greater refrigeration of the part than if it passed over a dry surface, and in the first case its influence upon the tissues of the skin, and upon the nerves in particular, must be more intense and deeper than in the second case. Furthermore, the energy of the action upon the peripheral expansion of a nerve, or upon the nerve trunk itself, is influenced by individual peculiarities. We may well conceive that by a certain degree of refrigeration other nerve tracts, particularly the sensitive and vaso-motor, may be put into a state of irritation through their connection with the chilled nerves. In this manner the influence of chilling may be more easily explained than by the assumption of an arrested exhalation of excretion products.

The dangerous effects of arrested perspiration were already known to SANTORIO (1614). There are experimental researches upon this subject by FOURCAULT (*Comptes rendus*, 1838); DUCROS (*Froriep's Not.*, 1841); BECQUEREL and BRESCHET (*Arch. gén.*, 1841, XII., p. 517); GLUGE (*Abh. z. Phys. u. Path.*, 1841); MAGENDIE, (*Gaz. Méd.*, 1846, Dec.); GERLACH (*Müller's Archiv*, 1851, p. 467); VALENTIN (*Archiv f. phys. Heilk.*, 1858, p. 433); BERNARD (*Leçons sur les propriétés phys. des liquides de l'organisme*, 1859, II., p. 177); and lately by EDENHUIZEN (*Zeitschr. für rat. Med.*, C. XVII., p 35).

The experiments undertaken by Edenhuizen upon various animals before or after shearing or plucking, by means of different substances (mucilage of gum arabic, linseed oil, linseed-oil varnish), showed that after smearing of the entire surface of the body, the animal, rabbits for instance, died in from 5 to 53 hours, after having exhibited the following symptoms: great trembling, extreme restlessness and dyspnœa, together with paralytic symptoms, tonic and clonic spasms followed by an apathetic state, with rapid diminution of body-heat, of the respiratory and cardiac movements. The urine was in most cases secreted in unusually large quantity, was of a high specific gravity, and sometimes, after a few hours, contained albumen. Examination *post mortem* showed hyperæmia of the muscles, the lungs, liver, and spl. en. more or less marked serous effusion in the serous pouches and in the subcutaneous connective tissue, ecchymoses of the gastric mucous membrane. Wherever the coating extended

the skin was found also hyperæmic. Upon its internal surface there appeared
a strong development of bloodvessels, which at the limits of the varnish coat showed
quite a distinct limitation to the covered parts. Numerous lymph-corpuscles were
found in the serous effusion of the connective tissue, and (also in the peritoneum of
most of the animals) crystals of triple phosphate ; these last being found even when
the examination was made immediately after death.

C. The moisture of the air. The atmosphere is never absolutely
dry. We call it dry, however, when it does not contain as much moisture
as it might contain at the existing temperature ; saturated when it does
contain as much ; and damp when relatively to its heat it holds much
water. At a higher temperature the air can take up much more water in
a given volume than at a lower. A warm air does not, however, seem
damp to us because much of the water it contains is in the state of vapor ;
a cooler air containing the same amount of moisture feels damp to us
because its water is easily condensed, the more so when the fall of tempera-
ture is sudden. The dew, the dampness of our clothing are indices not so
much of the absolute moisture of the air as of its cooling.

The air is dryest in the early afternoon, and moistest about sunrise.

Other things being equal, the body, *i.e.*, the skin and the lungs, exhale
more water when the air is dry, less when it is damp. In the latter case
the urinary secretion is more abundant, in the former scanty. A cold and
moist air withdraws much heat from the body, whereas a warm and dry air
increases the body-heat ; cold and dry air increases the expenditure of heat
from the body, and we feel much colder under these circumstances than in
damp air of a similar temperature. Cold dry air, by removing much fluid
from the blood, causes congestion of the lungs. Warm and damp air most
impedes the radiation of heat from the body through the skin and lungs,
causes exhaustion of the muscular and nervous systems, restrains the res-
piration, diminishes the appetite, impairs digestion, and increases the per-
spiration.

With reference to epidemics, no results have been obtained from the estimation of
the amount of moisture in air. Mortality, according to CASPER, seems to be less in
damp months, and greater in the dry (cold or hot) ; but this is only probably depen-
dent upon the extreme degree of heat and cold.
PETTENKOFER (in *Zeitschr. f. Biologie*, I., p. 181) discusses the *modus operandi* of
wet feet. If we come from out of doors with wet feet into a warm room with dry
air, a marked evaporation commences. If we have only an ounce and a half of
wet woollen material on our feet, the water it contains will need so much heat for
its evaporation that with it a half pound of water might be raised from 0 to the
boiling-point, or more than a half pound of ice melted.
Fog is made up of water molecules. It is not included in the moisture. It acts
principally as a cooling agent, and does not diminish the capacity of the air for the
absorption of moisture.

D. Composition of the air. The air which surrounds us, and which
we breathe, is seldom entirely pure, but is usually adulterated in a greater
or lesser degree. The substances mixed with it are mechanically or chemi-
cally injurious.

These facts are turned to practical account in the treatment by inhalation.

(*a.*) Mechanical impurities. Pulverized substances held in suspension
in the air seldom act upon the skin, but do so more often upon the con-
junctiva, where they produce irritation and inflammation. Their effect
upon the air-passages is, however, most important ; an effect frequently
observed. These particles are in part caught by the mucus of the tubes,

then expelled by means of the vibratile ciliary movement, and by hawking and coughing. A part, however, reach the air-vesicles, penetrate their epithelium and walls, and either remain imbedded in the interstitial tissue, or are carried by the lymphatics to the interlobular and subpleural tissue (even in false membranes accidentally present) and into the bronchial glands.

The inhaled substances are for the most part dusts, especially street-dust, chimney and lamp soot ; more seldom substances which are set free during the industrial development of their activity (coal-dust by workers in coals, by men employed in iron-works, by charcoal-makers ; sand-dust and particles of flint by stone-cutters and grinders ; fibres of flax, cotton, etc., by weavers ; meal by millers and bakers ; iron, and its oxide or protoxide by steel-grinders, goldbeaters, looking-glass polishers, and others ; tobacco-powder by tobacconists ; color particles by painters ; silicate of alumina by ultramarine-makers, etc.).

The proofs that these substances are inhaled are given in part by laryngoscopic observation, in part by the examination of the sputa, but chiefly by a study of the affected organ itself ; the identity of substances found in the organ, with those known to be suspended in the atmosphere being established by microscopical and chemical methods. This succeeds best in the case of certain characterized substances (charcoal, iron, silicates, etc.), while in the case of such as resemble the melanine grains derived from blood pigment, only an approach to certainty can be reached. And, lastly, the transportation of particles can be experimentally demonstrated ; for after it had been known that in animals subjected to the same conditions as man, a lung affection just like the human coal-lung was developed, experiments upon young, or confined animals gave the same result.

The consequences of the inhalations of dust-like substances depend upon their amount, their kind (sharp dust-particles, such as those of granite, steel, operate most injuriously), and the condition of the respiratory passages. They consist of, in the first place, irritation of those passages, with consecutive hawking and coughing, later in hyperæmia and catarrh of the bronchi. The substances imbedded in the lung-tissue proper, in small quantity, as in present conditions may be seen in human beings of all ages (the so-called lung pigment, anthrakosis of the lungs), do no particular harm. Larger quantities cause diminution of the respiratory surface, diminution of the elasticity of the lungs ; later we have capillary bronchitis, catarrhal or interstitial pneumonia (fibrous or purulent) with their complications, pigmental induration in the shape of small, very hard, shot-like nodules, which are sometimes colored black throughout, in part white in the centre—bronchiectasis, the so-called chronic tuberculosis : *pneumonokoniosis anthracotica, siderotica, chalicotica,* etc.

BUBBE, *De Spadone hippocratico lapicidarum Seebergensium,* etc. Halle, 1721.—RAMAZZINI, *De morbis artificum,* 1717.—PEARSON. *Phil. Trans.,* 1813, II., p. 159.—LAENNEC, *Traité de l'auscult. méd'cale,* 1819.—E. H. WEBER, *Hildebr. Anat.,* 1832, IV., p. 219.—GREGORY, *Edinb. Med. and Surg. Journal,* 1831, XXXVI., p. 389.—W. THOMSON, *Med.-Chir. Trans.,* 1837, XX., p. 230, 1838, XXI., p. 341.—GRAHAM, *Edinb. Med. and Surg. Journal,* 1834, XLII., p. 323.—BROCKMANN, *Die metall. Krankh. des Oberharzes,* 1851.—TRAUBE, *Deutsche Klinik,* 1860. No. 49 u. 50.—*Berlin. klin. Wochenschr.,* 1866, No. 3.—VILLARET, *Cas rares d'anthrac.,* 1862.—CROCQ, *Presse méd. Belge,* 1862, No. 37 ff.—LEWIN, *Beitr. z. Inhal.-Therap.,* 1863.—KUSSMAUL, *Arch. f. klin. Med.,* 1866, II., p. 69.—ZENKER, *Ibid.,* p. 116.—ROSENTHAL, *Wiener Med. Jahrb.,* 1866, XI., p. 97.—KNAUFF, *Virchow's Archiv,* 1867, XXXIX., p. 442.—SLAVJANSKY, *Ibid.,* 1869, XLVIII., p. 326.—MERKEL, *Archiv f. klin. Med.,* 1871, VIII., p. 206, IX., p. 66.—HIRT, *Die Staubinhalationskrank ,* 1871.

For the parasitic forms contained in the air, *vide infra.*

The various striking colors of the hair (green, red, blue) are produced by the deposit of various pigments (copper, indigo, etc.), and not by true chemical combinations.

β. CHEMICAL IMPURITIES.—The gaseous constituents of the air in open and in ordinary inclosed spaces do not undergo as much change as one might expect they would. The proportion of oxygen and nitrogen always remains the same (21 volumes of oxygen, 79 volumes of nitrogen) even in overcrowded rooms; there appear, however, in such places a small increase of carbonic acid, some ammonia, the fluid acids of the sweat, as well as occasionally the putrid organic substances of evaporation. The best known of these changes consists in the proportion of carbonic acid, of which normal air contains from 3 to 8 parts in 10,000. If the amount surpasses 1 per cent., the atmosphere becomes unhealthy; if there be more than $\frac{1}{2}$ per cent. it will do harm if long breathed.

Although it is certainly more healthy to breathe pure air, yet it cannot be said that definite diseases are produced by air made impure by human exhalations. If factory hands, children who overfill school-houses, look pale, are anæmic and scrofulous, it must also be borne in mind that they cannot procure many things essential to good health, such as nutritious food, etc.

The contamination of the air by large amounts of carbonic acid, carbonic oxide, hydrogen, ammonia, carburetted hydrogen, arseniuretted hydrogen, ether, chloroform, some of which act in a negative way (asphyxia by carbonic acid, nitrogen, hydrogen), others doing positive injury (carbonic oxide, carburetted hydrogen, sulphuretted hydrogen, arseniuretted hydrogen), will be treated of under the head of poisons.

Gases and mixtures of gases, in their relation to respiration, are divisible into four groups (VIERORDT, RANKE, HERMANN):

1. ATMOSPHERIC AIR.—This alone can be breathed indefinitely long. In unconfined spaces its composition is always found uniform, and even in closed rooms in which there are many persons congregated, the CO_2 cannot easily surpass 1%. PETTENKOFER found 1 part in 1,000 parts of air in a sitting-room without ventilation, in a lecture-room from 1 to 3, in a school-room 7 (others as much as 9.4), in a common room at an inn (after guests had been in it several hours) 4 to 5 parts. LEBLANC found in the parterre of a theatre 15 parts p. m. (per mille), in the highest part of the theatre 28 parts p. m. of CO_2 after the performance. As soon as air contains more than 2 to 3 parts p. m. of CO_2 it becomes offensive to us, by reason of the admixture of certain organic products of exhalation, whose exact nature is unknown.

CARL BREITING (*Vierteljahrsb. f. öff. Gesundheitspflege,* 1870, II., p. 17) has given us information concerning the increase of carbonic acid in school-rooms during the hours of instruction. In a school-room he found:

	At beginning of Hour.	At end of Hour.
From 8 to 9 A.M.	25	48 p. m. CO_2.
9 to 10 A.M.	47	69 "
10 to 11 A.M.	62	81 "
2 to 3 P.M.	55	76 "
3 to 4 P.M.	65	94 '

Small relative increase of oxygen occurs under a high barometer in cold weather; a diminution is observable in long, hot summers, in tropical climates, in mid-ocean, and upon high mountains. Greater increase of oxygen is made use of for therapeutical purposes in the so-called pneumatic cabinets (see p. 56).

2. GASES WHICH, WHILE NOT POSITIVELY INJURIOUS, DO HARM BY EXCLUDING OXYGEN.—Nitrogen and hydrogen, and, to a degree, carbonic acid. Asphyxia occurs because the inspired air does not contain oxygen enough to supply to the blood-corpuscles the quantity required for the maintenance of the normal composition of the blood. In an atmosphere composed of these gases, the sense of want of breath is felt as soon as blood issues from the lungs in a venous state; mammals are apparently

dead in 2 to 3 minutes later. In pure nitrogen gas, carbonic acid is separated from the blood, and nitrogen taken up, but only in small quantities. Similar phenomena are observed during the inhalation of hydrogen, and, to some extent, during that of CO_2.

3. MIXTURE OF GASES OF THE SECOND GROUP WITH OXYGEN.—If the nitrogen of the air be replaced by hydrogen, the animal continues to breathe without difficulty; an increase in the absorption of oxygen, as well as in the exhalation of carbonic acid and nitrogen, takes place, the hydrogen remaining almost unaltered. In a certain sense, protoxide of nitrogen is a substitute for oxygen. It may be inhaled in large quantities, causing exaltation symptoms, a condition like drunkenness, etc. Under these circumstances much of it is absorbed, and from its decomposition carbonic acid and nitrogen are given off.

4. GASES WHICH ARE POSITIVELY INJURIOUS.—They produce decompositions when taken into the blood; many, such as chlorine, ammonia, the nitrites, also produce strong irritation of the respiratory organs, abundant secretion from the bronchi, cough, and laryngismus. Among the most poisonous gases are carbonic oxide, carburetted hydrogen, sulphuretted hydrogen, arseniuretted hydrogen. Carbonic oxide, to which ingredient (10, 12, and more per cent.) illuminating gas owes its poisonous properties, unites with the coloring matter of the blood to form a carbonate of hæmoglobin, and by it oxygen is wholly driven out of the blood. Blood-corpuscles charged with carbonic oxide cannot take up any more oxygen; the blood is of a dark cherry-red color. The poisonous gases in privy-vaults are carbonic acid and sulphuretted hydrogen. The carbonic acid acts in part negatively, in part positively, by an action upon the central nervous system; it suddenly kills ganglion-cells. The sulphuretted hydrogen acts by losing its hydrogen, which forms water in the blood, thus setting sulphur free; the blood is at first yellowish green, later black.

OZONE deserves a special mention. It is, as is well known, a modification of oxygen, which has greater oxidizing power, and which is set free by every discharge of electricity, and also during sudden processes of oxidation, as, for example, when phosphorus is shaken with air even in the dark. Ozone plays an exceedingly important part in the animal organism in its relations to respiration.

It cannot be doubted that the blood-corpuscles carry the oxygen of the atmosphere into its chemical activity. A proof of this is afforded by the behavior of hydrocyanic acid. When it is introduced into the blood in small amount, it causes death by asphyxia, by bringing about a cessation of oxidation processes and metamorphosis of tissue; added in similar proportion to blood-corpuscles it destroys their capacity (which they have in the same way as platinum) of decomposing the peroxide of hydrogen. Hydrocyanic acid also destroys the power of blood-corpuscles to change the condition of oxygen, and thus demonstrates the very intimate relations existing between the corpuscles and this element. Hence follows the great importance of ozone in the vital processes.

Physicians are altogether too much inclined to connect the ozone of the air with diseases. Inasmuch as ozone irritates the mucous membranes, for a long time all epidemic diseases, particularly influenza, were thought to be dependent upon an increase in the amount of ozone. In the last two years the ozone contained in the air has been frequently and thoroughly investigated. These investigations have shown no special relation of ozone to inflammatory diseases, which it should have increased, and none to miasmatic affections (typhoid fever, cholera) in which it was thought it would be diminished.

Ozone may influence health by destroying fetid gases which develop from decomposing animals and vegetables. The therapeutical use of ozone against acute and chronic diseases, particularly the so-called septic diseases, has been of late again recommended.

e. THE ELECTRICITY OF THE ATMOSPHERE.

That lightning sometimes suddenly kills men and animals, sometimes lames and stuns them, is well known. Wounds are not always found in these cases. It is also known that the muscles contract when an electrical current is applied to them, or broken. It is a very different thing, however, with the electricity of the atmosphere and its degree of tension. Its influence upon health is very questionable, or at least little understood.

For a study of the electricity of the skin, see KLEMM, *Deutsche Klinik*, 1872, No 41, 48.

f. MOVEMENTS OF THE AIR.

A calm is dangerous, because during its continuance the products of decomposition of animals and plants, as well as marshy exhalations, are not dispersed. The warmer the air the more dangerous is the calm.

We call it a calm when, in the open air, the atmospheric current does not exceed one-half metre per second (PETTENKOFER).

A moderate wind is wholesome, since it purifies the air by promoting diffusion of its constituents. It occasionally becomes injurious by transporting dust and miasmata. Strong winds are dangerous for those having pulmonary diseases, because they render respiration more difficult.

The direction of winds is of interest, because upon that depend the heat and moisture of the air. East winds are cold, or cold and dry; northerly winds cold, and oftener damp than dry; westerly winds are damp; south winds warm, sometimes damp, sometimes dry. The influence of winds upon the conditions of some few healthy persons, and many persons with pulmonary disease, is very various. Their influence upon the development of disease is, however, very obscure. With north and easterly winds catarrhs are made worse; pulmonary diseases are set up during the prevalence of any other wind as well, and particularly on spring days with westerly winds, on cold days with an east wind. The dry south wind of southern countries called *Föhn* in Switzerland, *Sirocco* in Italy, *Chamsin* in Egypt, is very exhausting, and has a peculiarly evil influence upon new-born children and new-comers (immigrants).

g. LIGHT.

The optic nerves may suffer from too much and from too little light; and conjunctivitis may also be produced by dazzling by snow, or by sand particles. Excited or maniacal persons become calm more easily in the dark than in the light. We cannot positively say that light is quite as necessary for animal life as for the vegetable organization. It is true that persons inhabiting dark places, deep valleys, that chamber workmen become anæmic and scrofulous; and it has even been asserted that cretinism was caused by the darkness of narrow mountain valleys. Such questions are not so easily solved, because many other influences, such as dampness, insufficient food, etc., co-operate to produce the result

WINSLOW. *Light: its Influence on Life and Health,* London, 1867.—For the influence of light upon the development of various diseases of the eye, particularly myopia, consult COHN.

No other influence can be attributed to the sun than that of heat and light. This is very important for the preservation of health, inasmuch as the movements of the air of dwellings is facilitated by it, and by it the air is kept dry. Convalescents are always very comfortable in the sunshine.

We do not know of any effect of the moon upon the origin and course of disease.

The influence of weather and of seasons is made up of the already studied factors—heat, moisture of the air, etc. In the matter of climate (*vide infra*) we must, besides, take the soil conditions into account; and, besides, the kind of food, clothing, dwelling, have an influence which is not wholly to be eliminated.

As regards seasons and weather, the most important points have already

(see p. 60) been spoken of. Sudden changes are the most effectual conditions; thus there is an increase in the number of cases of disease upon the recurrence of the first cold of winter (pneumonia, especially in children and old persons); in the spring the first warm days with east and north winds (catarrhs, pneumonia); the summer time being, however, particularly dangerous, if cold nights succeed very warm days (cholera, dysentery).

In general it may be said, that damp, rainy, cool weather is healthier than fine weather with dry air; more severe diseases occurring in the latter condition.

2. THE SOIL.

The geognostic constitution of the SOIL exerts an influence upon man partly by the so-called soil-water which it contains, and partly by the drinking-water which flows through it.

Wherever there is not under us naked solid, impenetrable rock, we find water under a number of porous layers of earth. This water fills the pores of the strata in which it is; filling those in the lowest strata completely, excluding the air wholly, and is then called underground water; or, it lies in close relation to air as it does just above the surface of the underground water, in which case the layers are termed moist.

As a rule, the UNDERGROUND WATER is found in greater or less quantities upon the uppermost stratum which is impervious to water, and is usually sufficient to supply the wells of the locality. Usually it is found only in a single stratum, though we not rarely meet with another (or several) impermeable layer above the water, on top of which a moderate amount of water exists, at least temporarily—the so-called stratum water. This usually will not suffice for the feeding of wells, and often disappears in drouthy seasons. In the making of wells care is taken to traverse these sources of stratum water in order to reach the underground water proper. Even if stratum water be found in abundance, it is not usually fit for use, being often contaminated by its proximity to the surface. The depth at which underground water is found, varies from five to twenty to thirty metres and over. The impervious stratum upon which it rests is usually a clayey, moderately hard rock; upon this there are loamy and sandy layers of variable extent and thickness, interspersed here and there with clay, which allows of the accumulation of stratum water; next there is the so-called roller layer, made up of larger stones; above all lies the humus. All these layers are filled with air, are temporarily or, as a rule, more or less moist; the dampest layers are nearest the underground water, and are sometimes invaded by it. The amount of underground water at a given spot depends upon:—first, and principally, upon the amount of atmospheric precipitation; second, upon the flow of water from higher localities; and lastly, upon the amount of water in streams. Local complete absence of water is due to hilly or wave-like upheaval of the impervious strata; a superabundance of water is produced by a basin-like depression, in which the water of higher places accumulates. The abundance of water in a locality must of necessity vary at different times, according to the atmospheric precipitation and the flowing in from other sources. By means of repeated systematic measurements in various places, variations in the amount of underground water have been observed, especially since attention has been attracted to their importance.

The variations in the amount of underground water, which can be well repre-

sented for localities by curves, with tolerably regular abscissæ, have undoubtedly great influence upon the origin of certain epidemic diseases, especially typhoid fever and cholera. For example, the number of cases of typhoid fever in Munich (and apparently also in Berlin) increases with a diminution of the underground water, and decreases with its accumulation. Epidemics of cholera show themselves immediately after a considerable decrease of underground water has taken place. In these phenomena the important factor seems to be, that the disappearance of the water sets free a certain number of injurious decompositions of organic substances from the yet moist strata; these products being taken up by the air of the ground, and by it transported into human dwellings. It is in the highest degree doubtful that the underground water can directly exert, by carrying these substances into the drinking water, a morbific influence.

The air contained in the ground above the ground-water layers, occupies, as we can convince ourselves without a minute examination, a great space; it may equal and surpass one-third of the total mass of earth. This air is carried upward into our habitations, since it is never continuously still. It is set in motion by everything which can disturb gases, such as gusts of wind on the surface of the earth, changes of temperature, etc. And this mobility of the ground air is not diminished by the frozen hardness of the ground in winter, since the change of water into ice is not accompanied by any loss of porosity. A consideration of the relations of ground air to health, makes plain the great importance of scrupulous cleanliness in the vicinity of human dwellings, and the necessity of keeping the earth pure; points to which such extraordinary importance has been attached in recent times for the prevention of diseases. For filthy liquids which penetrate the ground must gradually undergo decomposition by chemical processes, and give origin to deleterious gases, etc., which may be carried into houses along with the ground air.

It is probable that the spread of cholera from house to house, in a given locality, occurs in some such way. In England it has been demonstrated on a large scale, that systematic purification of the ground, by the building of sewers, and by prohibiting the building of sunken or pit-like privies, exerted a most beneficial influence upon public health. By these means was brought about the cessation of murderous epidemics, and the mortality consequently diminished by an important amount.

It is probable that the CO_2 which is more abundant in the deeper strata, derives from organic processes which take place in the soil.

But it is not ground air alone which acts as a cause of ill health, for drinking water may under certain circumstances exert an evil influence, or at any rate it is often not without reason suspected of being a cause of disease. This is the more probable, if the water contain visible impurities, and especially if it be contaminated by organic substances (sewage.) Not less important is the surcharge of calcareous salt; this being the supposed cause of goitre, cretinism, etc.

With respect to goitre, we have the statement of FALCK relating to France, to the effect that it occurs more especially upon the following formations: the Lias, the upper new red Sandstone; their equivalents, the variegated Sandstone, and shell-limestone, the Permian and upper Magnesian strata. On the contrary, it very rarely occurs over primitive rocks, such as granite; on transition rocks, such as Grauwacke and Schist, the mountain limestone, Carboniferous strata; and also as seldom upon more recent formations, the Chalk and green Sandstone, with the various members of the Tertiary Group.

Water of marshes, when used for drinking purposes, most surely produces sickness; for example, malarial fever, in some places of a malignant type.

Another way in which the ground water operates injuriously is by satu-

rating the walls of houses, thus preventing the entrance and exit of fresh air ; in other words, dampness of walls is a great hindrance to ventilation. This condition is in great measure the cause of the great frequency of pulmonary phthisis in damp houses and localities.

This last point has been made clear, especially by English studies. Populations dwelling on dry, sandy soils, showed a small prevalence of phthisis, while the disease was very common in people living upon a damp, clayey ground. In fifteen English towns the mortality from phthisis diminished from 11 to 49 per cent. (!) after drying of the subsoil by means of proper sewerage.
[Consult H. L. Bowditch, *Consumption in New England*, Boston, 1862.—ED.]

Another interest attaches to the soil, that relating to its modification of atmospheric pressure, of the temperature, purity, dampness, and the movements of air, and to its influence upon the nature of food. In general, the inhabitants of mountainous districts are stronger and more enduring ; yet the higher we ascend the poorer vegetation appears, and man suffers chiefly in his nutrition, without being attacked by any special disease. Barren and bare elevated regions have delicate inhabitants, and we there meet even with intermittent fever alongside of goitre, cretinism, scrofula. The same is true of deep, elevated valleys. In low valleys there is a greater draught of air the straighter they are ; rheumatic affections prevail. In plains the irrigation is of especial importance. In the neighborhood of the sea the temperature is on the whole more uniform ; chilliness being more felt in many prevailing winds. The healthiest residence is upon the banks of a rapidly flowing stream. The most dangerous parts are lowlands and marshy regions, and this in proportion to the heat, as in summer and in the south. In such regions not only intermittent fever, but also cholera, dysentery, and catarrhal diarrhœa (especially in children), occur frequently, especially in new-comers. There is special danger in uncultivated regions, or where a previously fertile, peopled, and healthy section is desolated.

3. THE CLIMATE.

By climate is understood the sum-total of all influences derived from the atmosphere and soil. It is possible, from a consideration of these phenomena, to make a tolerably accurate estimate of the salubrity of a given climate. It is, however, further necessary to know the mortality and morbility * of a locality in order to proceed upon perfectly safe ground. It is further to be noticed that the totality of native inhabitants to whom the mortality reports refer, is often prevented by other than climatic conditions, as social or political influence, from sharing the advantages of the climate ; whereas an independent foreigner, who can procure the best lodgings and food, obtains the benefit of the climate and its healthful influences. This is true of many places in the south.

The chief influence of the ocean upon climate consists in its moderating the heat of summer and the cold of winter (the so called marine, or coast, or island climate).

The chief influences of forests upon climate are that wooded regions have cooler summers and warmer winters than those deprived of woods ; that daily variations of heat are less in forests ; that the forests so modify evaporation from the soil and leaves, that stationary strata of air just above woods are warmer than over barren soil, field or meadow.

* The German word *morbilität* is so correct a name for the condition that we venture to offer its literal translation as a new English medical term.—[ED.]

With respect to their peculiarities as adjuncts to medical treatment, climates have been divided into: (1) Alpine, (2) sub-Alpine, (3) midland, or indifferent, (4) marine climates. Into this classification there enter the great factors of atmospheric pressure, heat, and moisture. An Alpine climate may be designated as cool-dry, the sub-Alpine as cool-moist, the midland as warm-dry, and the marine climate as warm-moist.

A person beginning to live in a climate new to him easily becomes ill. The ACCLIMATION DISEASES, so called, are, apart from endemic and infectious diseases, nearly always gastric and intestinal catarrhal affections.

A new science, MEDICAL GEOGRAPHY, has sprung from CLIMATOLOGY. The geographical distribution of disease, if studied in relation with its causes, affords important results in pathology, in ætiology, and therapeutics. Compare MÜHRY, *Klimatologische Untersuch.*, 1858; and particularly HIRSCH, *Handb. der histor.-geograph. Pathol.*, 1859 u. 1860; BOUDIN, *Géog. médicale*, vols. ii., 1856; BLODGETT, *Climatology of the United States*, Phil., 1857.

The mortality of a district is to be measured by the proportion existing between the annual deaths and the number of inhabitants. If, for example, a city has 70,000 inhabitants, and 1,500 people die in it each year, we say that this city has a mortality of $1,500 : 70,000 = 15 : 700 = 1 : 46.6$.

There occurs in the north of Europe 1 death for each 41.1 inhabitants.
"   "   "   middle   "   1 "   "   40.8   "
"   "   "   southern   "   1 "   "   33.7   "

Among the diseases which prevail in more or less limited territories are the following:

The PLAGUE, that is, the oriental boil plague, which makes its appearance on the eastern shores of the Mediterranean, particularly in Constantinople and Cairo, about every ten or fifteen years. This disease does not prevail in summer and hot weather. It always ceases in Cairo during July, and has never passed the southern boundary of Egypt, the first cataract of the Nile.

YELLOW FEVER, an acute disease characterized by vomiting of blood, jaundice, and fever, is endemic in South America and the West Indies, being occasionally transported by means of vessels to Leghorn, Genoa, Lisbon, requires a temperature of 22° C. for its development, is found more upon the plains than upon mountains, yet may occur at an altitude of 2,000 feet and more. [It prevails almost every year in the Southern cities of the United States: Galveston, New Orleans, Baton Rouge, Mobile, Pensacola, Charleston, and even Wilmington. In a few seasons this disease was transported to Baltimore, Philadelphia, New York, and even Boston.—ED.]

TYPHOID FEVER, pre-eminently a disease of the temperate zone, appears in the north as well, but is there a much milder affection. It is to be found also in the torrid zone, but is there complicated by allied febrile states, whose anatomical characters have not yet been studied with precision, with the exception of the bilious typhoid fever of Egypt, which is accompanied by hæmorrhage in, and inflammation of the liver, spleen, and kidneys, and which does not exhibit any intestinal lesions.

EXANTHEMATOUS TYPHUS is occasionally as widely spread as typhoid fever; it is, however, more restricted to northern latitudes, especially in North America, Great Britain, Sweden, the Russian Baltic provinces.

MALIGNANT (CONGESTIVE) INTERMITTENT FEVER is to be met with in Hungary on the Danube and Theiss, in Italy on the Po, upon the entire west coast of Africa, in many parts of the United States and Central America.

CHOLERA is occasionally met with everywhere.

DYSENTERY occurs everywhere, but is especially severe in the south.

SCORBUTUS is a disease of northern climes.

SCROFULA appears in the northern part of the temperate zone.

TUBERCULOSIS shows itself throughout the inhabited parts of the earth, but is incomparably more frequent in the temperate zone, especially between 45° and 55° north latitude, than in the north or south. In all climates it is most common in populous cities, where human beings are crowded together; in the country, and in

thinly-peopled countries, in the Steppes of Kirgis, in countries surrounded by deserts, such as Egypt, Morocco, as well as in the Russian Baltic provinces, it is exceedingly rare; in St. Petersburg it again becomes common.

A change of climate exerts a favorable influence upon patients suffering from all kinds of chest diseases, rheumatism, anæmia, and upon convalescents in general, when they go to a warmer, or more especially a more equable climate. In Germany the following resorts may be named: Wiesbaden, Baden-Baden, Baden-weiler, Botzen, Meran; in Italy, Pisa, Rome, Palermo; in France, Pau, Nice; in Africa, Egypt, Algiers, Madeira; in the United States, Minnesota, Colorado, New Mexico, parts of California, Jacksonville (Florida,) Aiken (S. C.;) Bermuda, Samana.

4. THE DWELLING.

The dwelling may be considered as a sort of private climate, which is voluntarily limited. It is of greater importance to health the more the inhabitant remains at home; more important for the northerner than for the southerner, who remains more in the open air. Especially noteworthy are those buildings in which men are congregated for a long time; factories, hospitals, schools, dormitories. Even healthy persons spend a good third of their lives in the last.

The characters of a good dwelling are: sufficient size of the room, upon which depends the purity of the air; dryness of the floor and the walls, and to a certain degree of the air also; an exposure in our climate, when possible, to the east and south; good ventilation without constant draughts of air; location in a healthy region; the protection of blinds, etc.

Fresh, pure, that is, oft-renewed air, is an important *desideratum* for sick and well persons, particularly for such as are obliged to spend many hours daily (in school-rooms), or months and years (orphan asylums, garrisons, prisons), in the same building. The air becomes impure by insufficiency of the space in which the human beings remain, by the want of, or by imperfect ventilation, by injurious mechanical and chemical admixtures.

The size of the space needed by man, healthy or sick, when living in an inclosed place, cannot be determined with absolute accuracy. The average has been variously placed at 300 to 800 cubic feet, in different countries, and under very various conditions (in barracks, hospitals, etc.).

The size of the space is of comparatively less importance when a careful and regular ventilation renews the air in it from time to time.

It has been determined by experiments upon respiration, that a man needs six cubic metres (160–170 cubic feet) of space to enable him to breathe an hour without being injured by his own carbonic acid, or by the rarefaction of the air.

It has been specially ascertained that each child needs 1.5 cubic metre;
    that each child in the company of old people needs 3.0   "
    that each adult in the company of old people needs 8.0   "

This is exclusive of lighting and heating, which consume much oxygen; and in the estimate the space occupied by the furniture must be taken into account. The number of hours during which a space is to be used, must determine an increase in every dimension of the space, so that for example a dormitory for four persons holding at least 200 cubic metres of air, with a height of 12 feet, should be about 24 feet long and 18 wide.

The evils inherent to smaller rooms are deficiency of oxygen and accumulation of carbonic acid. As the effects of these conditions are but gradually developed, it is impossible to name any particular diseases, besides

anæmia, scrofulosis, tuberculosis, to which the inhabitants of small dwellings are liable.

The remaining gross impurities of air cause for the most part debility or irritation of the mucous membrane. Among these are to be named sulphuretted hydrogen, hydro-sulphuretted ammonium, aqua ammonia, which abound in water-closets and privy-vaults, as well as in kitchen sewers, and which, especially when the dwelling is heated, ascend to the rooms; empyreumatic oils during lighting with ill, imperfectly burning substances; volatile acids from human or animal exhalations; carbonic oxide, which benumbs at the development of smoke in coal combustion, and quickly kills; carbonic acid (see p. 65). Strong substances in a state fit for inhalation, such as the perfume of many flowers, are injurious to many persons, particularly those of a nervous disposition.

According to PETTENKOFER, to whom we owe many researches upon the question of ventilation, an average man expires each minute 5 litres of air, which contain 4 per cent. of carbonic acid; in each hour 300 litres, including 12 litres of carbonic acid. That air alone is healthy which, after the sojourn of men in it, contains at the highest 5 parts per thousand of carbonic acid. In order to secure the thorough renovation of the air in the inclosed space, a large amount of fresh air is necessary. In order that the air should remain good, it is necessary that there should be introduced at each moment two-hundred times the volume of the expired air; and, as a man expires about 300 litres in an hour, there must hourly enter 90,000 litres or 60 cubic metres of fresh air. In rooms where sick or well persons stay for any length of time, this is to be secured only by means of judicious ventilating appliances, best by the direct entrance of fresh air, not as well by removal of the impure air. This purpose is attained by the constant opening of numerous and large windows, as in the American pavilion and tent system.

PETTENKOFER has further shown that the dry walls of our houses, particularly those of brick, and also those of rag-stone (the latter particularly when plastered), are permeable to the air, and that lime and gypsum plastering, and oil painting, do not prevent this penetrability. The innumerable minute pores of the wall, by means of which the air in the room communicates with the outside air, allow the entrance of much more air than can come in through the leaks and cracks of doors and windows. Every impact of air upon the external face of a wall causes a movement in the air on its inner face. The amount of interchange of air through the wall depends especially upon the difference in the temperature of the atmosphere on the outside and on the inside: the greater this is, as for example in the cold winter season, the more air enters and leaves a dwelling in this way. The porosity of walls is destroyed at once by wetting: hence the disadvantages of new, ill-dried dwellings. Natural ventilation is somewhat increased by open fire-place heating of rooms, but not very much, as is usually assumed.

While a certain number of noxious gases exhibit specific odors, or produce unpleasant sensations in the mucous membranes of the eye, larynx, etc., there are others, as for example carbonic acid, carburetted hydrogen, which are not perceptible to the smell.

The manner of heating, of airing, the closure of windows, the care of the surroundings of the house, etc., belong to HYGIENE. Dwellings with damp grounds and walls are above all deleterious; they are colder, their walls are less porous, they are favorable to the occurrence of putrefaction and mouldiness, and the moisture of the air itself may act directly. It is certain that rheumatism and neuralgia follow upon the operation of these causes.

The greatest demand for reform comes from public institutions of all kinds, all public offices, orphan or foundling asylums, lying-in hospitals, hospitals for the insane, general hospitals, almshouses, and prisons; because into these buildings most persons go unwillingly, and because the State, which in a manner despotically lodges them, is in duty bound to provide for their health.

In making plans for buildings, the following allowance of ventilation per person, per hour, should be made.

60–70 cubic metres in hospitals for ordinary cases.						
100	"	"	"	"	"	wounded patients.
150	"	"	"	"	"	epidemic diseases.
50	"	"	"			prisons.
60	"	"	"			ordinary workhouses.
100	"	"	"			workhouses for invalids.
30	"	"	"			day barracks.
40–50	"	"	"			night barracks.
40–50	"	"	"			theatres.
30–60	"	"	"			assembly rooms.
12–15	"	"	"			schoolrooms for children.
25–30	"	"	"			" adults.

Unfortunately these requirements are not always fulfilled, even in enlightened states. This is more especially true of prisons. The great mortality in them is in part due to unavoidable causes. On the average it amounts to 1 : 20–30, in particularly well-managed institutions 1 : 40, which is higher than the general mortality, although there are no new-born children which increase the mortality ratio so much. The most common diseases of prisoners are tuberculosis, pneumonia, typhoid fever, mental affections. The food and the kind of work of course play a part in increasing mortality.

The mortality of large cities is larger in summer and autumn than that of the open country, and in winter is a little less. In large cities the inhabitants, at least those without means, suffer from crowded dwellings. Besides, harm is done by the emanations of the ground upon which the houses are closely packed, and whose subsoil is saturated by the filtration of human excrements, with organic putrid substances, or with contagious material, as for example that of cholera, typhoid fever, etc.; by the absence of vegetation, which clears the atmosphere of superabundant carbonic acid ; by the air stagnating in narrow streets, by its making streets turn cold, or warm and moist ; smoke and dust are present in large quantities ; food is often adulterated ; sewers become dangerous if they carry off much refuse, cemeteries, slaughter-houses, gas-houses, if they give off bad odors. On the other hand, well-governed large cities have these advantages, that sanitary regulations are better executed by the authorities, and that in time of distress help is nearer and is more freely given. In small towns and in the country the indifference of individuals toward ordinances is usually greater ; physicians and institutions are not numerous enough, and the disadvantages of the locality appear at their worst.

In the last ten years the morbidity as well as the mortality of many large cities has been diminished, by the erection of water-works, by suitable sewerage (partly through the so-called flood-canal system [*Schwimmen canal-system*], and the water-closet system, with air- and water-tight traps).

5. CLOTHING AND BEDDING.

The clothing with which civilized people and the northern races cover themselves, is to be studied from the following points of view respecting its usefulness or injuriousness.

Our bodily frame is to be looked upon as a warm and moist body exposed to the air, which loses heat in three ways : by radiation, conduction, and

evaporation. By covering the skin with clothing we prevent direct loss of heat, and diminish the contact of the air with the body surface; we cause a diminished loss of heat in all the three ways.

A great advantage accrues in the heating economy of the body from the fact that heat is not lost in only one way, because the action of the several modes renders possible a delicate regulation of the loss of heat. What we lose by one way is equalized by diminished loss in the other two ways. On the average the loss by radiation and conduction is the most constant under similar circumstances, and the evaporation of moisture is the means of partly balancing the differences existing in the amount of heat produced, as well as the errors caused by functional disorder of the other channels.

The loss by RADIATION may be a very important one; fifty per cent. of the total heat being usually separated in this way. This loss increases with the difference between the temperature of our body and that of the surrounding medium.

Consequently, we feel cold in a room which is not warmed throughout, especially at its periphery, though the air near us be at the pleasant degree of 20° C. Radiation is also notably diminished where our body is surrounded by objects of a similar temperature; as for example, in a space crowded with human beings, or in a crowd in the open air; and we feel warm under such conditions, even if the thermometer shows but a moderate degree of heat, and this because our neighbors are as warm as ourselves. In compensation for deficiency of radiation we begin to perspire, and try to cool ourselves by means of fans, the heat escaping by the other two ways.

The loss of heat by CONDUCTION is also important. So long as our body is warmer than the air which surrounds us on all sides, so long does our body heat it. No equalization of temperature can, however, take place in this way, because the heated and rarefied air rises to a distance from the body, is replaced by colder air, which in its turn goes off when heated.

This ascending air current may be so strong as to influence the wings of a sensitive anemometer placed beneath the clothes: this being a current unnoticed by us because our nerves cannot appreciate air in motion at a speed of half a metre per second. The loss of heat by conduction becomes much more important if we exchange badly-conducting air for one that is slightly heated, or for the much better conducting medium water. Whereas we can comfortably remain in moderately warm air with only light clothing on, we are very cold with the same clothing in water of a similar temperature, although in the latter case loss of heat by evaporation has wholly ceased, and the loss by radiation is reduced to a minimum. Cool baths cause a much greater loss of body heat than exposure in an equally cold atmosphere. In the open air we lose much more heat by conduction than in a room, because the movements of the air are much diminished by the walls, and consequently a much less quantity of air passes over us in a given time, in a room, than in the open air. The minimum of heat lost by conduction in a room must be compensated by loss from radiation and evaporation. By the use of a fan in a room the volume of air passing over us is increased, and with it the loss of heat by conduction.

Of how much importance EVAPORATION is for the cooling of the body, may be inferred from the fact that one gramme of water renders latent 560 heat-units in its passage to the gaseous form. An individual while inactive will lose in this way according to experiment, 900 grammes of water by the lungs and skin—that is, 504,000 heat-units; one exerting himself violently, 2,000 grammes of water, or 1,120,000 heat-units. This explains why the blood never becomes warmer, in spite of active exercise (apart from a certain excess). The organism brings about this result, in so far as it concerns the skin, by the changing activity of its vaso-motor nerves (vari-

able according to need), by means of which the moisture of the skin is
diminished or increased. So long as we are surrounded by air, there co-
incides as a rule, with a greater loss of heat by conduction, an increased
evaporation at least as long as the circulation in the skin remains active,
and the air is not wholly saturated with moisture. Consequently we be-
come cool much more easily in a dry than in a moist atmosphere, because the
saturated air can no longer withdraw heat from our bodies by evaporation,
while dry air does this in an extreme degree.

Very interesting also is the cooling of the body by respiration in air of varying
temperature and moisture. If we set down the volume of air which an adult individ-
ual in- and expires in twenty-four hours at an average figure of 9,000 litres, we ob-
tain the following by calculation :—
An adult loses in twenty-four hours by the breathing of :

Air at   0° C. (dry),   293,040 heat-units.
  "   30° C. (dry),   274,050   "
  "   0 C. (moist), 265,050   "
  "   30° C. (moist), 105,390   "

That is to say, that the loss of heat is much more important in dry air than in air
saturated with moisture. At a temperature of 0° C. at the point of complete satu-
ration, the loss is about 28,000 heat-units, or quite 10 per cent. less; and at a
temperature of 30 C. at the point of complete saturation, the loss is 61 per cent.
less than at the point of greatest dryness.

Death is at last brought about by extreme loss of heat, and a degree of
such a loss, beyond a certain endurable limit, gives rise to disease, by cool-
ing. The increased loss of heat may affect the whole or a part of the body;
as for example, when we step into a cold room when covered with perspira-
tion, or when we remain much too long in a cold bath, or if we sit near a
cold wall, an open window, etc.

By means of our clothing, we receive back, after a while, a part of the
heat which without it would radiate from it to other neighboring bodies,
because the stuffs out of which it is made are not diathermanous, allowing
heat-rays to pass through unabsorbed. Still, the heat absorbed by the
clothing may radiate from its outer surface, just as it might radiate from
the uncovered skin. "Our clothes freeze for us." The passage of heat
through this covering depends essentially upon the conductibility of the
cloth, and upon its thickness, i.e., upon the distance which the radiating
heat must traverse in order to reach the outer surface of the clothes, and
upon the time necessary for this transit. At the same time we heat, by
means of this heat radiating from the body, the immediate surrounding
of our body, viz., the stratum of air lying between the skin and the cloth-
ing; and this is constantly done in a greater or lesser degree, as needed
to protect our nerve-terminations from the unpleasant or injurious effect
of sudden changes of temperature in their immediate vicinity. We thus
lose our body heat through rightly-chosen clothing in such a way that we
feel comfortable. In proportion as the loss of heat increases, while the
internal production remains about the same, we experience the necessity of
allowing the escape of heat from the vicinity of our body to take place
more slowly. Then, if through the independent activity of the vaso-motor
nerves of the skin a marked degree of restriction of the loss of heat is
brought about for a certain time, the repression of the peripheral circula-
tion no longer suffices, partly because of the exhaustion of the nerves,
partly because of the amount of loss. Supported by a large experience, we
then put on several articles over one another, and what happened to the
skin when covered by the first set occurs to the second set of articles, and

to the third; with the increase of the number of clothes there is an addition of warmed layers of air in the neighborhood of the nerve-endings.

Clothing cannot be defined as articles destined to keep the air away from the body, for, on the contrary, we wear no clothes which do not allow of a continual ventilation of the surface of the body. The stuffs which serve to make our warmest clothing are much more permeable to air than those which we designate as cool. A current of air is constantly passing through the clothing, the volume of which, as in every kind of ventilation, depends upon the size of the apertures, upon the degree of difference between the air within and that without the clothing, and upon the velocity of the air about us. Clothing tempers the contact of air with our body, only by preventing the impinging of the air as a moving body against the nerves. Clothing also regulates the temperature of the air by causing it to assume a mean degree of heat by passing through the pores of the cloth; a mean of 24 to 30 C. " We carry about us in our clothing in the open air, even in northern regions, the air of the south. We feel in this just as we should feel standing naked in a perfectly calm atmosphere of from 24° to 30° C."

According to the investigations of KRIEGER (*Zeitschrift f. Biologie.* V., p. 476) there is but little difference between individual substances in their capacity for radiation. KRIEGER filled a cylinder of tin with warm water, surrounded it with various kinds of cloths, in various ways, and noted the diminution of heat at stated intervals. If wool be put down as having a capacity of 100, then that of chamois is 100.5; silk, 102.5; cotton, 101; and linen, 102.

The color of the fabric is also without essential influence upon radiation. It is otherwise in the matter of absorption of heat by differently colored cloths. And indeed in this respect (absorption), the difference in the same colors, between different textures, is not important (cotton, 100; linen, 98; flannel, 102; silk, 108), although marked for the same fabric in various colors. In different colored shirtings, 100 being the absorption index of white, that of pale yellow is 102; deep yellow, 140; pale green, 155; deep green, 168; turkish-red, 165; pale blue, 198; black, 208. These figures are for the effects of exposure to direct heat.

KRIEGER investigated in how much the loss of heat by radiation was retarded when several layers of the same fabric were drawn tightly one over another, and he noticed in double layers a radiation of—

3 % in thin silk,	9 % in thick linen,
4 % in gutta-percha,	10–12 % in chamois,
5 % in shirting or fine linen,	14 % in flannel,
6 % in thick silk,	16–26 % in winter kid leather.

In other words, if 100 heat-units passed out in a given time through a single layer of silk, only 97 heat-units escaped through a double layer (tightly drawn) of the same material. These surprisingly small differences are an evidence of the retardation of the loss of heat by friction in the radiation through the second layer of cloth, whose pores are precisely similar to those of the already thoroughly heated pores of the first cloth, and form in reality only the continuation of those pores. In other respects the differences between fabrics are not so much dependent upon weight and solidity as upon their shape and volume. If, however, KRIEGER drew only the first layer of cloth tightly around his tin cylinder, and allowed the second to hang at a distance of from .5 to 1 cent. from it, somewhat after the fashion in which we wear our external clothing, he noticed a much more marked diminution of the loss of heat, to wit: for linen, an increase of 32 %; for shirtings, 33 %; for silk, 32 %; for flannel, 29 %; for chamois, 30 %; for gutta-percha cloth, 36 %. Thence follows the very important proposition, that we may be much more or much less warmly clad with the same amount of clothing, according as we wear it tight or loose. The cause of this difference is the thickness of heated layer of air inclosed between the clothes.

It is not alone the stratum of air inclosed between the skin and the clothes which plays an important part in preventing loss of heat, but the air included in the fabric itself—the air entering into its texture.

PETTENKOFER has investigated the question of the permeability of various fabrics by means of glass tubes, one end of which was closed by pieces of the cloth to be tested, while he forced air through them. Through pieces of similar areas, in similar times, the air passed in the following relative amounts, flannel being considered

as 100 : through linen of medium thickness, 58 ; through silk fabrics, 40 ; chamois, 58 ; tanned white leather, 1 ; samian leather, 51. The protecting effect of clothing does not either depend upon the degree to which it keeps the air off from us, otherwise kid gloves would be 100 times warmer than flannel, which, as is well known, is not the case. Other fabrics containing much air are, as well as flannel, well adapted to keep us warm ; as for example, fresh cotton-wadding (in contradistinction to that which is old and compressed), and fur, with its delicate hairs to which the air clings. KRIEGER shaved fur, and found that its power of giving off heat was increased in the proportion of 100 : 190. The dry skin of shaven fur is, however, always a little porous ; if it be covered with linseed-oil varnish its power of transmitting heat rises to 258, and by means of a coating of gum-arabic it reaches 296. Shaven and varnished fur-bearing animals die through refrigeration (the freezing-death), if no heat be given them from without. The more delicate the hair of the fur, the more warmly it covers, because the heat leaving the body is so much better retained by it. In a good fur animal, however, the body-heat is not greater in summer than in winter. In the winter the equilibrium between the temperature of the skin and that of the air is found near the root of the hairs ; in summer it takes place near their free ends. Impermeable fabrics do not possess these good qualities of fur, and are consequently used as clothing only for special objects. They allow of the penetration of no dampness from without, but cause the retention of the fluids of evaporation, and restrict the circulation of air in the underlying clothes. Water-proof coats are good only to shield us from the wet; they make us moist by the retention of perspiration ; they are useful only in wet weather or in great winds, not in wet and warm weather, or in a calm atmosphere.

The more the air of a tissue is displaced by water, the less it can keep us warm, because it becomes a much better conductor of heat. Hence the ease with which we " catch cold " in wet clothing ; hence the susceptibility to dampness. If we go out into a cold and dry open air, we do not, *pari passu*, feel as cold as in equally cold but damper air.

We must not undervalue the importance of this. PETTENKOFER chose two equal pieces of linen and flannel, as representatives of the most important animal and vegetable fabrics, dried them at 100° C., at which point they lose nearly all their hygroscopic water, and weighed them in accurately-closing tin boxes of known weight. They were then exposed to air at various degrees of temperature, from time to time replaced in the tin boxes, and weighed with all necessary precautions. In this way the variations in weight—in other words, the amount of water taken up hygroscopically by linen and wool—were easily ascertained. For example, in twelve hours the following quantities of water were taken up by 1,000 grammes of the following fabrics :

	Linen.	Wool.
At 1°. 2 C. in lecture room....................	74 grm.	143 grm.
" 3°. 1 C. in cellar.........................	77 "	157 "
" 4°. 4 C. in cellar.........................	111 "	175 "
" 12°. 2 C. in laboratory.....................	63 "	105 "
" 19 . 0 C. in room.........................	41 "	75 "

If we estimate the weight of a woollen suit of clothes at 10 lbs., the amount of hygroscopic water contained in it, consequently, is 1½ lb., which quantity will require for its evaporation 420,000 heat-units.

Under all circumstances wool contains more hygroscopic water than linen, and retains it also much better. Consequently the changes in the amount of water contained in linen are more rapid than those in wool during the evaporation of water in dry, and the acquisition of water in wet weather.

Both substances exhibit similar relative properties during wetting by, or the drying of fluid water. Linen is easily saturated with water, and water escapes from it quickly ; wool loses water slowly, but it takes up much more than linen. Water evaporates more rapidly from a linen than from a woollen surface, which latter yields up its water in a regular way, as is shown by the following table. 1,000 grammes of linen soaked in water, then pressed until no more water could be forced out of it, retained 740 grammes of water ; and 1,000 grammes of flannel treated in the same way retained 913 grammes. The surfaces of these equal pieces of tissue were like-

wise equal. Both cloths were hung up to dry in a heated chamber, and the water retained in them—

						Linen.		Flannel.
After 15 min. in temp. of 20°		C. amounted to	521 grm.		701 grm.
" 45 "	"	20°	C.	"	380	"	603	"
" 75 "	"	19° 5 C.		"	229	"	457	"
" 105 "	"	19°	C.	"	99	"	309	"
" 135 "	"	19°	C.	"	55	"	194	"

It is easy to understand that fabrics as a whole, by the partial stoppage of their pores by water, lose their permeability to air when they become wet. Coarse tissues with large pores remain longer pervious to air; with substances of similar porosity, the adhesion of water to the fabric determines whether it shall close its pores slowly or quickly, temporarily or for a long time. Linen, cotton, and silk are quickly hermetically sealed by wetting; while wool does not become so, or only after saturation. As the porosity of all tissues depends mainly upon the elasticity of their fibres, it is of the highest importance whether it be the same in the damp and dry states, or how much it may vary under these conditions. A character which distinguishes wool from the other three substances, is that its fibres retain almost all their elasticity when wet, whereas other fibres lose theirs almost wholly. It is because the air is more driven out of linen or silk fabrics than out of woollen ones, that we catch cold more easily by being wet while clothed in linen or silk. Similarly wet woollen stockings do not produce cold feet as easily as wet linen ones. On the other hand this peculiarity of silk and linen is of advantage when it is desirable to keep the body warm and dry. By means of linen shirts we efficiently remove heat and a moderate amount of evaporation from the skin; while profuse perspiration is best taken up by a woollen tissue.

A very important article of clothing (since in it we pass a great part of our lives) is the BEDDING. The bed is not merely a place of rest, but also a cover during sleep. Bedding is made of the same materials as day-clothes; those used next the skin, of linen, silk, and cotton; the underlying parts, of animal fibres, feathers, wool. The bedding must be at the same time warm and airy: we heat the bed with our body just as we do our clothes, and in its turn the bedding heats the air which traverses it from below upward. The layers which regulate the heat are thicker than those of ordinary clothing; this is required, because in the absolute rest of sleep tissue metamorphosis is much reduced, and less heat is produced: moreover the air is more thoroughly heated in horizontal layers than in the erect position of the body. The bed is a most important apparatus for the preservation of body-heat; since the heat of the bed keeps up the circulation of peripheral parts without great waste of tissue, thus relieving the internal organs, which are thus enabled to rest. Whoever, for several days in succession, cannot lie in bed, does not feel rested, but often also experiences changes in his temperature. Beds are, particularly in cold weather, indispensable to well-being; they, in a certain degree, take the place of food. Light bed-covering is advisable for young people, because much heat is apt to increase the sexual appetite and lead to onanism.

Under certain circumstances clothing may be also useful for the purpose of shielding the body from heat-rays; as, for instance, hats in summer. The mode of its operation in such cases is just the same as has been described above.

Weight is an element to be considered in clothing, because heavy articles, if they be bad conductors, overheat the body by the exertion necessary to

bear them. The same element should be kept in view in the matter of bed-covering; it should not be so thick and heavy as to interfere with the respiratory movements, or unnaturally increase perspiration.

" Our clothes are the weapons with which man combats the atmosphere, in so far as it is dangerous."

Articles of clothing may press upon and injure the organs over which they are placed. In women there are often found transverse depressions in the liver with opacity of its capsule, and atrophy of its tissue, produced by corset, and petticoat bands. Moreover, excessive lacing produces disproportionate breathing with the upper thorax. The pressure of shoes produces various diseases of the soft parts and bones.

Compare PETTENKOFER, *Zeitschr. f. Biologie.*, 1865, I., p. 180, and *Beziehungen der Luft zu Kleidung*, etc., 1872.

6. FOOD AND DRINK.

Leaving out medicines and poisons, the consideration of which belongs to pharmacology and toxicology, we can divide ingesta into nutritive and pleasing materials.

Only such substances can serve as nutritive materials whose constitution is similar to that of the tissues of the body, or, at any rate, such as contain the elements needed by the tissues, such as nitrogen, carbon, hydrogen, oxygen, sulphur, phosphorus, iron, chalk, potassa, soda, etc. It is well known that the animal organization does not form the majority of its proximate principles, such as albumen and related bodies, fat and sugar, out of the elementary bodies, but that the substances must be exhibited in an organic or complex form, from which they are eliminated.

Food may be noxious because too little or too much of it is ingested; and, besides the form and mass, the temperature and quality, the uniformity (with respect to the proportions of animal and vegetable ingredients) of the food, as well as, lastly, the irregularity in the time of eating, are injurious.

For the condition of absolute fasting, as well as for the effects of withholding important articles of diet, see paragraph on the anæmia of inanition.

The evils brought about by the shape and amount of ingesta, of solids as well as fluids, belong to special pathology, because the lesions and disturbances produced are local.

The temperature of food and drink is a cause of disease only in that it may lead to refrigeration of the stomach, and with respect to the possible evil effects of cold drinks. More rarely, in childhood particularly, we meet with burning of the upper part of the digestive tube, and consequent inflammation of these parts, and of the upper air passages.

The quality and ill effects of food belong more properly in treatises on diseases of the digestive organs. The general consequences of spoiled food resemble those which follow upon the use of too little food. Water which claims to be " healthy pure drinking-water " must not be chemically pure; it should, on the contrary, contain certain ingredients, and only a minute quantity of other substances in order to be harmless. At any rate, it must be clear. A water which contains visible impurities is not to be regarded as good drinking-water. Even after filtration water may be dangerous to drink, because some of the injurious ingredients may remain in solution. This is the reason why filtered river water which is furnished by the water-

works of many towns is not healthy, or not at all so compared with clear, fresh spring water, which should alone be used for this purpose. The pleasant taste of the latter is produced by the presence chiefly of CO_2. It contains salts, as follows: chiefly chloride of sodium, sulphate and carbonate of lime in small quantities, so that the result of dessication of 100,000 parts of water never exceeds 50 parts, or 0.0005. If the mineral ingredients exceed 0.4 p. c., or 0.004, the liquid is called MINERAL WATER.

The most important impurities of drinking-water, particularly in that drawn from pump-wells in populous districts, are nitrates, especially in combination with ammonia; abundant chlorine combinations, and, lastly, organic substances of animal or vegetable nature. Such impure water, in order to be still drinkable, must not contain in 100,000 parts more than 0.4 parts of nitric acid, 0.8 parts of chlorine, and 5.0 parts of organic matter. Boiling does not much improve such water. These impurities reach the drinking-water mainly through sewage water, which filters down to the wells. They produce principally gastric and intestinal diseases, and probably also sometimes typhoid fever.

That the above named impurities may, under certain circumstances, set up infectious diseases, particularly typhoid fever, is proven by quite a number of old and recent observations; although this is denied at the present day by competent observers. (Compare, on the first side of the question, BIERMER, *Ueber Enstehung und Verbreitung des Abdominaltyphus*, in VOLKMANN's *klinische Vorträge*, 1873, No. 53; on the other side, *Ueber die Aetiologie des Typhus*, *Vorträge von BUHL*, FRIEDREICH, v. GIETL, v. PETTENKOFER, etc. 1872.)

At any rate, it will be admitted, that to provide pure drinking-water is one of the most important principles of hygiene; hence the number of projects for establishing waterworks to conduct spring water into large cities. Whether a water is pure is to be determined only by chemical means; particularly the taste is an unreliable test, since waters containing too much saline matter, and consequently unfit for use, may taste very pleasantly. In doing this it is by no means necessary to make an exact estimate of each element of the residue of the water.

RADLKOFER (*Zeitschr. f. Biol.* 1865, I., p. 26) has made a thorough examination of the organic substances present in the wells of Munich.

Under the name of delicacies we separate from the foods a class of substances whose ingestion is not necessary to the reconstruction of the tissues, which are not themselves present in the body, but which must satisfy a deep need of human nature, because they are almost universally used. To this class belong alcoholic drinks, coffee, tea, betel, tobacco, coca, etc. Even the most primitive races employ one or other of these substances, of which it can only be said that they sometimes excite, sometimes depress the nervous system, and somewhat retard tissue metamorphosis; and also that, under certain circumstances, their use may cause serious disease of the nervous system, and later, of other systems. A consideration of these substances individually is here out of place.

[Consult: PARKES, *Manual of Practical Hygiene*, Lond., 1864; REICH, *System der Hygiene*, 1870-1; HAMMOND, *A Treatise on Hygiene*, Phila., 1863; PEREIRA, *On Food and Diet*, 1843.—ED.]

7. OCCUPATION, PROFESSION, AND OTHER SOCIAL CONDITIONS.

It is not in the province of pure aetiology to determine the importance of the first condition, for the result to which the occupation leads depends largely on the degree of success attained, and a number of delicate persons are never called to any business.

The question comes up for consideration from general points of view. Poisons, in the form of powder or vapors, which sometimes act only in a mechanical manner (as in millers, watchmakers, stone-cutters, grinders), sometimes chemically (powder of poisonous metals in foundry workmen, lead-powder in type-moulders and house-painters,—among gasmen): compare p. 64. By too great or too restricted movements of the body, with consequent effects upon the muscles, bones, respiratory and circulatory apparatus; the long maintenance of certain attitudes, as standing in compositors, which leads to varicose veins; as the bending forward of the thorax and the prevention of complete lung expansion, in shoemakers, tailors, and weavers, leading to congestion of the lung apices, producing tuberculosis or emphysema; confinement to a room, in small, badly ventilated, and over-crowded manufactories, and other work-rooms; or remaining in the open air without sufficient protection against temperature and dampness; or a frequent change of place while in a heated state, by which workmen are made peculiarly liable to pulmonary diseases; over-exercise of the muscles, producing atrophy of these organs and other consequences; straining of the respiratory organs, as in performers upon wind instruments, criers, clergymen, teachers, conducing to pharyngitis, laryngitis, pulmonary emphysema, etc. In addition we must recognize a number of more or less accidental influences incidental to the occupation, as is the case with inn-keepers, brewers, wine-merchants, fishermen, drivers, commercial travellers, and especially soldiers.

The mortality in European armies in time of peace ranges from 1.5 to 2 per cent.; whereas in the males of the same ages in the civilian population it is only 0.8 to 1.2 per cent.

Intellectual callings are as a rule healthy, especially if the mental labor can be pursued in a degree of comfort: clergymen, professors, merchants, lawyers, live to a very old age. Other intellectual occupations which necessitate emotional excitement and a free, if not quite regular life, more quickly wear out the individual; as in the case of politicians, artists, actors. On the other hand, philosophers and mathematicians, who are often ill-nourished, reach on the average advanced age. Teachers and physicians, as shown by statistics, die earlier than others who are put in the class of intellectual workers. The most fortunate are those whose occupations oblige them to take a good deal of exercise, as farmers, officers in times of peace, waggoners, woodmen.

The mortality of the various professions is much better understood than their morbility. CASPER, *Wahrscheinliche Lebensdauer*, 1835. LOMBARD, *De l'influence des professions sur la durée de la vie*, 1835. NEUFVILLE, *Lebensdauer und Todesursachen*, u. s. w., 1855.

Civilization has been accused of having brought along with it an increase in morbility, and in the number of diseases. This may be; and yet, with improved culture and an increased number of physicians, mortality has not increased.

In Geneva, according to the estimates of ODIER and MALLET, the probable duration of life of the newly-born, was five years in the 16th century, twelve years in the 17th century; from 1701 to 1760, twenty-seven years; from 1761 to 1800, thirty-two years; from 1801 to 1813, forty-one years; from 1815 to 1826, forty-five years. In the twentieth year of life the probable survival was, in the 16th century, twenty-two years; in this century, forty years. At the thirtieth year it was, in the 16th century, nineteen years, and thirty-two in the 19th century. At the sixtieth year there is

first observed a more equal time of probable survival in all centuries. In one hundred years the probable length of life of new-born children has increased from 6 to 26 years; in Berlin, from 23 to 28 years. In Berlin all ages show the improved viability. The marked improvement observed during this century, depends principally upon the better care of young children and the introduction of vaccination. The losses by war, though affecting the strongest individuals, are subordinate; even women now live to a greater age.

According to other authorities the above results depend upon errors, because the calculations were made chiefly in a few large cities. If the general mortality has diminished in Sweden, France, and other countries, during the last one hundred years, and the average of life increased from two to seven years, it is in consequence only of a diminution in the births and in infant mortality. In Prussia the average length of life has not changed since 1816, and in England not in one hundred years. Even if the duration of life has somewhat increased, we must not conclude that the actual greater vitality and vigor of nations is proven, or even made probable. At any rate, infant mortality alone has decreased. Well-to-do people live much longer than the poor.

According to CASPER, out of 1,000 poor in Berlin, one-third died in the first five years of life, whereas, out of 1,000 well-to-do persons, one-third had not died at the fortieth year. One half of the poor survive the age of thirty years, and one half of the rich that of fifty.

In England the Peers are extraordinarily favored; the gentry (nobility in general), stand, in respect to longevity, far above merchants, and the merchants above the working people. Among the latter the agricultural laborers are better placed than the factory workmen. In general, the influence of comfort and affluence upon the prolongation of life, is most marked in infancy and in old age. Naturally, this general statistical result does not exclude the occasional survival of individuals of the lower classes to an extremely unusual old age.

Usually, we take adult persons of the poorer classes to be from five to ten years older than they really are.

Lastly, it has been likewise statistically demonstrated, that marriage—without regard to early or late marriage—has an extraordinarily favorable influence upon the duration of life. The regular life which the married state carries with it, together with the better care of the individual during illness, are favorable to longevity. This is apparent in both sexes, but more so in the male sex. The difference of probable survival in the married over the unmarried, and especially the widowed, is quite important.

According to CASPER a married man has the prospect of becoming sixty years old, while a bachelor must be content with forty-five years of life. Whereas, one quarter of married men reach the age of seventy years, only one-twentieth of single men attain it. In this connection we should remember, however, that very many men die between the ages of twenty and thirty years; that on the whole few men marry before thirty, and that consequently the number of married men dying between twenty and thirty must be relatively very small. Among the insane and suicides, from two-thirds to three-fourths are unmarried. Similar results have been reached by DEPARCIEUX, ODIER, and others.

8. PARASITES.

SWAMMERDAMM, *Bibel der Natur. Uebers.*, 1752.—VAN DOEVEREN, *Abh. v. d. Würmern im menschl. Körper. Uebers.*, 1776.—GOZE, *Vers. einer Naturgesch. der Eingeweiden. thier. Körper*, 1782.—ZEDER, *Anleit. zur Naturgesch. der Eingeweidewürmer*, 1803.—RUDOLPHI, *Entozoorum hist. nat.* 1808–10.—BREMSER, *Ueber lebende Würmer im lebenden Menschen*, 1819.—SCHÖNLEIN, *Müll. Arch.*, 1839. p. 82.—STEENSTRUP, *Ueber d. Generations-Wechsel*, 1842.—SIEBOLD, *Arch. f. Naturgesch.*, 1835, I., p. 59; Art. *Parasiten* in R. WAGNER's *Hdwörterb. d. Physiol.*, II., p. 640, 1844.—DUJARDIN,

Hist. natur. des helminthes., 1845.—VOGEL, *Ally. path. Anat.*, 1845, p. 385. —BERTHOLD, *Gött. Nachr.*, 1849, No. 13.—V. BENEDEN, *Les vers cestoides ou acotyles*, 1850.—DIESING, *Systema helminthum*, 1850–51.—ROBIN, *Hist. natur. des Vegetaux parasites*, 1853, with Atlas.—WEDL, *Grundz. d. path. Histol.*, 1853.—KÜCHENMEISTER, *Die in und an dem Körper des lebenden Menschen vorkommenden Parasiten*, 1855.—VIRCHOW, *Arch.*, 1856, IX., p. 557.—GERVAIS and VAN BENEDEN, *Zoologie médicale*, 1859.—DAVAINE, *Traité des entozoaires et des maladies vermineuses*, 1860.—PASTEUR, *Ann. de chim. et de phys.*, 1860. C. LXIV., p. 1 ; *Ann. des sc. nat. zool.*, 1861. D. XVI.—BÄRENSPRUNG, *Ann. d. Char.*, 1862, X. 1 H., p. 37.—R. LEUCKART, *Die menschl. Paras. u. die von ihnen herrühr. Krankh.*, 1., 1862, u. 1863, II., 1 Lief., 1867 ; 2 Lief., 1868.—KÖBNER, *Klin. u. exper. Mitth. aus. d. Dermat.*, 1864.—HALLIER, *Jen. Ztschr.*, 1865, p. 231. *Die pflanzl. Paras.*, 1866.—M'CALL ANDERSON, *On the Paras. Affect. of the Skin*, 2 ed. 1868.—KARSTEN, *Chemismus der Pflanzenzelle*, 1869.—NEUMANN, *Lehrb. d. Hautkrankh.*, 1870.—EIDAM, *Der gegenw. Standpunkt d. Mycologie*, 1871. —ZÜRN, *Die thier. Paras. auf u. in d. Körper unserer Haussäugethiere*, 1872.—COHN, *Beitr. z. Biol. d. Pflanzen.*, 2 H., 1872, p. 127.—STEUDENER, *Volkm. klin. Vortr.*, 1872, No. 38.

PARASITES are animal or vegetable organisms which spend their whole life, or certain periods of it, or live only temporarily upon or within another living organism, for their nourishment or development.

PSEUDO-PARASITES are those parasites which only casually happen upon man, because they here find moisture, warmth, and organic substances in decomposition (many fungi and infusoria).

Of many organisms is it questionable whether they are parasites or pseudo-parasites.

A. VEGETABLE PARASITES.—PHYTOPARASITES.

The vegetable parasites occurring in the human body belong to the cryptogams, and to the fungi and schizomycetes. A number formerly classed among the algæ, are now known as lower development-forms of fungi. Exceptionally perhaps, the sarcina is an alga.

CRYPTOGAMS are those plants which without preceding visible blossom and fruit propagate by means of simple cells, or cell-groups (spores, germ-granules), and which develop immediately, or in form of a sprout, into a new individual. Those cryptogams which interest us are (in opposition to the vascular and leaf-forming cryptogams) the so-called cell or frond-plants—the thallophytes ; the frond or thallus represents in the organization root, stem, and leaf.

Aa. FUNGI.

In the class of fungi belong those frond plants which have no chlorophyll in their cells, and receive their nourishment only from previously organized matter, and are therefore incapable of forming all of their organic ingredients out of inorganic matter ; which take oxygen from the air, and in return secrete carbonic acid. With respect to the second trait, these are distinguished : true parasitic fungi, which draw their nourishment from the fluids of living organisms ; and those which live only on decaying substances (saprophytes, carrion-fungi).

The whole vegetative body of fungi, the THALLUS, consists (a few doubt-

ful cases excepted) of filiform, more or less branched elements, the fungus-filament or hyphen. These grow at the extremities, and the terminal cell is always the only one to divide. The two principal members of the thallus are: 1. A part diffused within or upon the substratum, to take and store up nourishment: the ROOT-FROND, MYCELIUM or RHIZOPODIUM: 2. the bodies springing from it, which bear the propagating organs; the fruit-bearers or FRUIT-FILAMENTS (*stipites*, *pedunculi*).

The MYCELIUM possesses neither in itself nor in its filaments special peculiarities, so that it is difficult or impossible to determine even approximatively, to which species of fungus a sterile mycelium belongs. Especially is this the case with most parasitic fungi. The fruit-bearers support the organs of reproduction. The latter represent the cells, which are the germs of new individuals (SPORES, etc.), as well as the mother-cells from which they are generated (asci, etc.). The fruit-bearers consist either of a single fungus filament (FRUIT-FILAMENT, fruit-hyphen), or they form a compound fungus body (fruit-body).

The propagation of fungi is in no case through spontaneous generation, but takes place partly in an asexual, partly in a sexual manner. The former only is of interest to us. The fungus spores are developed in three ways: by free cell formation (the mother-cells are called asci, thecæ, spore-pouches); by constriction (the mother-cells are called basidians); by a growth-like or vegetative process; cell-fission or gemmation (the mother-cells are called sporangia). The mature spores are either movable (*swarm-spores*, ZOOSPORES), or motionless. The former embrace proportionately few fungi: they are naked, protoplasmic forms, without a distinct cellulose membrane, from whose surface two vibrating cilia, at the most, spring forth. All of the remaining spores are without independent motion: they have at the time of maturity, or even earlier, a permanent cell-membrane which consists of an outer layer (episporium), and of an inner layer (endosporium).—Most spore membranes are characterized by their great resistance to decomposition and strong reagents, especially concentrated mineral acids. The contents of the spores consist of a mass of protoplasm, homogeneous or containing in variable quantity, granules, oil globules, and vacuoles, and are usually without a nucleus. The spores are so developed that the membrane first bursts, and the contents protrude in the form of a pouch; this germ-pouch elongates more and more; receives a sheath and branches, and thus forms the mycelium. It is in the fresh state largely composed of water; when dry, it actively imbibes moisture from the surrounding medium.

SPORES ARE THE CHIEF MEANS OF THE GREAT SPREAD OF FUNGI. Their small size and lightness make it possible for them to spread everywhere, not only in liquids, but also through the air. The examination of dust, of particles in the atmosphere, of human and animal se- and excretions, also the special experiments of PASTEUR, and others, have shown that fungus spores capable of development are present everywhere.

The principal conditions for the growth of fungi are: moderate warmth (0–40° C.), moisture, some oxygen, stagnant and seldom renewed air, and organic substance. Light is unnecessary. Many fungi grow only in specific liquids.

The quantity and quality of the nourishment and surrounding media, exercise great influence upon the form and mode of fructification of fungi. In one medium the mycelium increases greatly, while in another it diminishes to the finest filament; with one food the fungus pushes forth vigorous spores, with another it constricts the

spore pencil, with a third it divides into yeast fungi. Upon this depends the so-called *pleomorphism* (TULASNE) ; *i.e.*, the same plants can occur under two or more forms, as well with respect to the organs of vegetation as to those of fructification.   Also the weather, amount of water, etc., have an influence upon the increase, etc., of fungus. —HALLIER has recently given the theory of TULASNE an undue importance ; BONOR-DEN rejects it ; DE BARY assumes an intermediate position.

The pathologically important fungi belong to the following groups :

DUST OR GERM-FUNGI, CONIO- OR GYMNOMYCETES.

They consist of single, clustered, or loosely connected spores of one or more cells, which germinate and develop into a filiform mycelium, out of which spores are formed by constriction.   These not uncommonly happen upon the same plant in two different forms.   With this there may also be forma-tion of so-called conidia, or secondary spores.   Here belong the rot and grease, as well as the rust of grain, and probably the several fermentation or yeast-fungi.

MYCODERMA (*Cryptococcus, Hormiscium, Saccharomyces*).
BEER-YEAST (*Mycrococcus* or *Cryptocroccus*, or *Torula cerevisiæ*) con-sists of large (0,004–0,008 mm.), round, or oval colorless cells which con-tain one, less often two, bright nuclear bodies resembling oil-globules. Mycelium is wanting.   From these cells new cells arise by a process of budding.   The new cells arise either by constriction, two clinging together, or many new ones bud forth, so that an entire row of cells hanging one to another is formed, but which are not transformed into proper filaments. The former is a sub-form which is found during fermentation at a temper-ature less than 10° C., the latter a higher form, which occurs at a temper-ature above 10° C.   They are found in diabetic urine, and in the contents of all parts of the digestive canal from the mouth to the anus (coating of the tongue, vomit, diarrhœic stools)—Their pathological significance is still doubtful.

WINE-YEAST (*Myc. vini*).
VINEGAR-YEAST (*Myc. aceti*).
MILK-YEAST (*Oïdium lactis*).

The last can grow fungus-like, if submerged, while upon the surface a mycelium of cylindrical articulated filaments arises, from which shoots grow up into the air, whose long cells separate easily.   The milk-yeast be-comes similar to higher forms of beer-yeast, when it comes in contact with solutions of milk-sugar in a confined atmosphere.   It is found upon sour milk, and especially in the acid fermentation of milk-sugar, where lactic acid is forming.

Several opinions concerning the nature of the yeast-fungi prevail.   Some (SCHWANN, PASTEUR, and others) consider them organisms *sui generis*, which arise in fermentable liquids from their own specific germs.   According to BAIL, BONOR-DEN, HALLIER, HOFFMAN, and others, they are only conditions, especially of mould fungi occurring in fermentable liquids, particularly the spore-forms, or sprouts of fungi, which in the atmosphere fructify in other forms ; they originate likewise from spores, it may be from yeast-cells themselves, or from other forms developed in the air, when they reach a liquid.

Filamentous fungi, Hyphomycetes.

The mycelium of these fungi consists of lengthened, tubular cells strung to one another in various ways, which form filaments and often present very elegant, regularly branched figures. The spores originate within the filamentous parts, or on the end of them, and at maturity become free by constriction. Here belong the fungus of the muscardine of the silk-worms (*Botrytis bassiana*), the potato disease (*Fusisporium solani*), the wine-grape disease (*Oïdium Tuckeri*), mould, the fungi of diseases of the skin and mucous membranes.

Mould-like forms are: *Penicillium glaucum, s. crustaceum,* common mould, pencil-mould.

It forms the greatest portion of the mould commonly occurring upon almost all vegetable decomposing substances (*e.g.* bread, fruit), more rarely of that occurring upon animal substances. The erect fruit-bearers, cross-partitioned, are raised upon a septate, abundantly and irregularly branched, colorless mycelium. The points are tufted, and upon the ends of the branches are formed numerous awl shaped sterygmata; each of these becomes constricted into a long chain of spherical conidia, which at first are connected, and furnish the pencil-shaped appearance.

Aspergillus glaucus, bluish-green mould, club-mould.

Found widely spread, especially on old wood as a fine cobweb-like growth. It is frequently found with the foregoing form. It consists of a similar mycelium. The fruit-filaments thereon, almost perpendicular, and mostly inarticulate, are expanded at their free extremities into a club-shaped basidian, on which sterygmata appear encircling it, and which by constriction furnish series of greenish, fine bristly spores.

With aspergillus there occurs on a mycelium the *eurotium herbariorum,* once thought to be distinct. Since both belong together, the fungus is now called *eurotium aspergillus glaucus.*

Mucor mucedo and *mucor racemosus,* often found on excrement and old articles of food. The bladder-like swollen fruit-hyphen (columellæ) are upon an abundantly branched, long-filamentous mycelium, which with age becomes septate. The abundant spores become free by the bursting or dissolving of the wall of the sporangium.

Bb. cleft-fungi, schizomycetes (*Bacterium, Micrococcus*).

These belong to fungi, as far as they are cellular plants, which are wanting in chlorophyll, and do not assimilate carbonic acid; but they are distinguished by the want of mycelium, and of basidian and ascan spores. Their increase is only in an asexual manner, by budding. Their distribution is extraordinarily great. Common atmospheric air, as well as water of all kinds, except fresh distilled water, even snow water, and that from the melting of pure ice, contain their germs. The tissues and fluids of the normal human body are free from them, with the exception of the skin, and easily accessible mucous membranes.

Historically noteworthy are: Leeuwenhoek, O. F. Müller; of all others Ehrenberg (in 1830 first introduced the family of the *Vibriones ;* in 1838 the four genera: *Bacterium, Vibrio, Spirochæta, Spirillum*); also Dujardin, Pasteur, Hallier, Nægeli, Cohn.

The name, *Schizomycetes* (Nægeli), is suggested by the great fragility of the

formations. The name *Bacteria* (HOFFMANN, and others), is used by many synony-
mously.

The classification of bacteria with fungi is differently received by different authors :
most probably they are to be separated from them (NÆGELI, DE BARY, HOFF-
MANN, COHN), in opposition to HALLIER, who regards them as yeast-forms, or
microeoceus-swarms of certain fungi (penicillium, etc.)—Consult NÆGELI, *Botan.
Ztg.*, 1857, p. 760. COHN, *Nova. act. acad. Leop.*, XXIV. I. *Botan. Ztg.*, 1871, p.
861.

With respect to the extraordinarily great importance which the schizomycetes
already enjoy as causes of individual diseases, as well as the confusion which exists
in the botanical and pathological data of this chapter, I prefer, in the following
botanical portion, to follow almost entirely the most recent work of COHN.

According to HOFFMANN (*Botan. Ztg*, 1869. No. 15-17), the kinds of schizo-
mycetes brought forward by EHRENBERG, DUJARDIN, PASTEUR, and others, pass
into one another; peculiarities which are to be held as characteristic of the species,
and which in various ways change in the course of development as there are changes
in the external conditions of life. H. includes in the bacterian series five forms :
monads, rods, vibrios, leptothrix and zooglöa. All these are found to appear to-
gether in infusions; those which have been putrifying for months, are richer in
the larger forms than those which have undergone decomposition only for a short
time.

BACTERIA are cells destitute of chlorophyll, with a globular, oblong or
cylindrical, twisted or curved form, which increase exclusively by trans-
verse division, and vegetate in an isolated manner (single-cell bact.) or in
cell-families (filamentous bact.) Bacterian cells possess a nitrogenous,
mostly colorless protoplasm, which is more strongly refractive than water,
and for the most part contains shining fat-like granules. The non-albumi-
nous but cellulose-like cell membrane is not destroyed by potassa and am-
monia, nor by acids, and resists putrefaction for a very long time. One
group of bacteria forms jelly-like masses (zooglöa), the other group consists
of bacteria which are freely dispersed, or occur in swarms.

In the globular and rod-shaped bacteria, the daughter-cells are, as a rule, separated
immediately after division ; sometimes, however, the cell-generations remain con-
nected, whilst their cell-membranes swell up into jelly-like limpid intercellular sub-
stance, and are united into larger, sharply-defined, elastic, supple, jelly-like masses;
ZOOGLÖA, COHN. These constitute diffuse or formed, irregularly globular, clustered or
pouch-like, lobed or branched jelly-like masses swimming in water or spread out
upon a substratum, and in which bacterian cells are inclosed in varying proportions.
In these jelly-like zooglöa the bacteria divide still farther ; when especially rapid
increase takes place, the young cells are very closely pressed against one another,
and the intercellular substance is little developed ; later the cells separate. To
the naked eye the jelly-like masses appear as colorless floccnli swimming in water,
which are deposited upon the external surface, walls, or bottom of a vessel, when
greatly increased, forming jelly-like masses, or thick gristly membranes of many cent.
in circumference. If the water contains iron in solution, this is readily precipitated
as an oxyhydrate, and the jelly is colored reddish-brown. If sulphuretted hydrogen
is generated in this water, the rusty-brown zoogl.a are blackened as in spoiled well-
water. The bacteria cells, imbedded in the jelly-like substance, do not perish, since
they not only increase very greatly, but also easily free themselves by solution of the
jelly, and then they swim freely in all directions in the water. The filamentous and
screw-bacteria never occur in jelly-masses, but scattered or in swarms.

The formation of swarms occurs in all bacteria, if they congregate within a
liquid in consequence of abundant nourishment, or hungering for oxygen rise to the
surface of it in endless multitudes. The bacteria swarm is distinguished from the jelly-
like zooglöa by the fact that the cells of the latter are immovably cemented by the
intercellular substance. On this account the zooglöa in water have a sharply defined,
for the most part spherical contour, which appears so much the more distinct, be-
cause the bacteria cells are more densely deposited on the walls of the jelly-like mass,
than in the middle of it. The bacterian swarms, on the other hand, exist merely as
free, movable cells, but which often are so densely congregated that they almost
come in contact, thereby forming a mucous mass; in moving water the individual

cells disperse, since they are held together by no intermediate substance. In fresh water the bacterian swarms lie for the most part near the surface, often in a large mass, one centimetre thick and almost oleaginous, which penetrates like slimy-gum into the deeper thin portion of the liquid. On the surface of liquids, in which bacteria propagate, there are, as a rule, very thin iridescent pellicles, in which motionless bacteria are often very regularly arranged in parallel rows. The pellicles are distinguished from the zooglœa by the fact, that in the latter the cells are united into globular masses by intercellular substance, whilst in the former, only a simple layer is present without intermediate substance.

Another form in which bacteria appear, is that of a pulverulent precipitate. As soon as the nutritive material in a liquid is exhausted, the farther increase of bacteria is arrested, and the little bodies are gradually precipitated to the bottom of the vessel; the liquid becomes clearer, earliest at the surface, the white powdery mass at the bottom becomes thicker and denser. All kinds of bacteria are indiscriminately mixed in the precipitate; they are only partly dead, for the most part they are in a state of quiescence, like yeast-cells in a fermented liquid.

Most bacteria exists in a movable and a motionless state. The movement consists in a rotation about the long axis, to which in the longer and more supple forms are also added active and passive movements, and stretchings in the direction of the length of the filament, never spiral movements. Motion appears connected with the presence of oxygen; in the absence of oxygen the condition is one of rest. The motionless state is lasting, if the bacteria are united into jelly-like masses or pellicles; in globular and certain filamentous bacteria motion is never observed.

It is doubtful whether spore or conidian formation takes place in bacteria.— Consult RINDFLEISCH, *Virch. Arch.*, 1872, LIV., p. 396.

Bacteria (especially *bact. termo*) develop and increase in an extraordinary manner in a so-called nutritive liquid, which is free from albuminous compounds and sugar, but contains besides a certain quantity of mineral substances (phosphoric acid, potassa, sulphuric acid, lime and magnesia) only ammonia, or tartaric acid: the former is the nitrogenous, the latter the carbon source of bacteria. Tartaric acid may also be supplanted by any organic compound of carbon, with the exception of carbonic acid.

I. GROUP: SPHERO-BACTERIA.—GLOBULAR BACTERIA.

(PASTEUR'S *Monas*, or *Mycoderma*. EHRENBERG'S *Monas crepusculum* and *prodigiosa*. HOFFMAN'S *Monas crepusculum*. HALLIER'S *Micrococcus*.)

GLOBULAR BACTERIA are spherical or oval cells, mostly under 0,001 mm. in size, without granular contents, with a membrane possessing a double contour. The cells are connected in pairs, and at the point of division are deeply constricted. By progressive division there are formed short chains of 3, 4 to 8 and more parts, which are stiff and bent, and, in consequence of the constrictions, moniliform. Or, the chains are irregularly broken, zigzag, and thus there are formed dense and confused accumulations of cells, colonies, which consist of a great number of cells, and are irregularly arranged with respect to one another. Or, finally, the daughter-cells arising from this division into twos, do not arrange themselves in chains, but at once form irregular deposits beside the mother cells, and are connected with them by intercellular substance. Thus are formed masses of numberless globular cells, which form jelly-like, often very tough, fibrous, drop-like, or membranous mucous masses. This mucous formation is the normal form assumed by those kinds which appear in pathological processes, and which cover the diseased organs in a dense layer, or are deposited into the interstices of the tissues. (This condition corresponds to the zooglœa-form of the rod-bacteria, but is distinguished from it mostly by the less development of intercellular substance; in consequence of which the

globular cells are closely pressed together, and present under the microscope an extremely characteristic, closely punctated or finely granular, shagreen-like appearance.)

It is difficult to distinguish globular bacteria from the amorphous, pulverulent, molecular deposit (detritus) of the most various organic and inorganic substances (carbonate and oxalate of lime, resin, india ink, but especially from fatty and albuminous substances.)

KYBER (*Dorp. med. Ztschr.*, 1872, III. 1 H., p. 44) regards as vegetable forms only those isolated granules which are provided with cilia. The granules of granular coagulated fibrin dissolved by the addition of acetic acid, the molecules of granular degenerated hepatic and renal epithelium, the granules generated in hyaline, mucus by acetic acid, the pigment molecules of the choroid—all have a globular nucleus and their incessant motion, the Brownonian molecular movement, is not to be distinguished from the movement of the micrococcus. Most of these granules are dissolved or rendered pale in acids and caustic alkalies more easily than the micrococcus, only the pigment granules of the choroid are more resistant than the latter. The arrest of the movement by the action of concentrated acids and caustic alkalies leads K. to conclude, that the little bodies having become softer, and the medium simultaneously more dense, the movements produced by ordinary jars of new currents in the fluid escape our senses, but with a high magnifying power are seen as a lively trembling or turning. K. holds the vital movement of the micrococcus not to differ from molecular movement generally.—Consult also LEX (*D. Ztschr. f. öff. Gesundheitspfl.*, 1872, IV., p. 47).

Besides by their form and movement, globular bacteria are to be distinguished from rod-bacteria by their function.

1st Genus. Micrococcus, Cohn.

Cells colorless or slightly colored, very small, globular or oval, united by transverse division into short moniliform filaments of two or more members (*mycothrix, torula-forms*), or into many-celled families (colonies, balls, heaps) or into mucous masses (*zooglöa-form, mycoderma-form*), WITHOUT MOVEMENT.

To this genus belong the following three " physiological species," since the distinction as to form and size is very difficult.

a. PIGMENT BACTERIA ; *chromogenic globular bacteria ; chromogenic forms of micrococcus*, globular bacteria, which appear in colored jelly-like masses.

They vegetate in the form of zooglöa (mycoderma of PASTEUR). They form mucous masses, which in consequence of a very quick cell-increase, develop in a short time upon the surface of their sometimes liquid, sometimes solid, mostly organic nutritive substance ; and they are sometimes completely enveloped in colorless mucus. Pigment occurs only in contact with air. All create an alkaline reaction. Air always contains germs of these bacteria. The generation of pigment is not a result of external conditions (variety in nourishment, etc.), but of specific and transmitted peculiarities.

α. INSOLUBLE COLORING MATTERS (red and yellow).
1. *Micrococcus prodigiosus*, COHN (*monas prod.* EHRENBERG. *Palmella prod.*).

Causes of the seeming blood-spots which sometimes during moisture appear on wafers, bread, potatoes, etc.

2. *Micrococcus luteus*, C.

β. SOLUBLE COLORING MATTERS (orange, green, and blue).
3, 4, 5, 6. *Micrococcus aurantiacus, m. chlorinus, m. cyaneus, m. violaceus.*
These do not belong to the globular bacteria which color milk blue and yellow, and pus like verdigris (*vibrio synxanthus*, etc. EHR., *bacteridium æruginem* SCHROETER).

b. ZYMOGENIC GLOBULAR BACTERIA.

7. MICROCOCCUS UREÆ : ferment of the urine ; ferment of ammoniacal fermentation.

From the researches of PASTEUR, V. TIEGHEM and COHN, it appears that fresh acid urine, after having stood exposed for two days at a temperature of 30° C., is cloudy from development of globular bacteria, which separate as globules or oval cells, swim about, or become connected by twos, fours, eights, chain-like (torula-form) etc. Later, rod and filamentous bacteria also appear.

c. PATHOGENIC GLOBULAR BACTERIA : " ferments of contagion."
8. MICROCOCCUS VACCINÆ (*microsphæra vaccinæ*, COHN).

Researches of ZÜRN, HALLIER, KEBER, WEIGERT, COHN.

9. MICROCOCCUS DIPHTHERICUS, according to many the cause of diphtheria (*vide ifra.*)
10. MICROCOCCUS SEPTICUS (*microsporon septicum*, KLEBS), according to many the cause of pyæmia.

11. MICROCOCCUS BOMBYCIS (*microzyma bomb.*, BÉCHAMP).

The cause of a very destructive epidemic among the silk-worms of southern France, but altogether different from *muscardine* and *gattine.*

The micrococcus especially has in later years been the subject of the most zealous inquiry. It appears in microscopic investigations with extraordinary frequency, some specimens almost everywhere, when they are looked for in a not entirely fresh part of the body ; it is probably also constant in some contagious general diseases. If the micrococcus happens in great quantity within a bloodvessel, it is most easily recognized by its disposition, by the peculiar smallness, the brightness, etc., of its individual elements. It is not changed by alcohol, ether, chloroform, caustic alkalies, and not too concentrated acids. Iodine colors it yellow ; carmine and hæmatoxylin sometimes color it, sometimes not. If, on the other hand, the micrococcus occurs singly, or in too small numbers free from or within cells, the distinction between it and other forms of molecules is often impossible.
LÜDERS and HENSEN (*Arch. f. micr. Anat.*, 1867, III., pp. 318, 342) found in the blood of healthy dogs, which had been withdrawn with all precaution, after it had stood for three days at 40° C., vibrios, while in the same blood which had been kept cold, they were found wanting. KLEBS (*Arch. f. exp. Path.*, 1873, I., p. 31) with like precautions failed to find them in the blood of healthy dogs.
A complete isolation of micrococci has not yet been possible ; the demonstrating experiments of many have not been successful in the hand of others. CHAUVEAU, as well as BURDON-SANDERSON, submitted vaccine lymph to the operation of gravity ; the uppermost layers were altogether inoperative, the deepest (which contained the fungi) very effective. TIEGEL (*Ueb. d. fiebererreg. Eigensch. d. Microsp, sept.* Bern, Diss., 1871) sought to separate by filtration by clay cells, the corpuscular elements from fluids of gangrene of the spleen containing bacteria, as well as from septic fluids. BERGMANN (*D. Ztschr. f. Chir.*, 1872, I., p. 396) found that by freezing and thawing out a liquid containing bacteria, the liquid becomes separated into layers, and the surface to the depth of some lines is free from bacteria. M. WOLFF (*Med. Centralbl.*, 1873, Nos. 8, 9) found by the ZAHN-TIEGEL method of filtration, a few bacteria and micrococci always present in the filtrate : it contained, after three or four days as a new cultivation the organisms in great abundance. The clay-cells thus do not prevent the passage of bacteria. WOLFF likewise had little success with BERGMANN's freezing method for isolation of bacteria, as well as with repeated filtrations.
KLEBS (*Arch. f. exp. Path.*, 1873, I., p. 31) experimented with the cultivation of his *microsporon septicum* in isinglass glue. These experiments differ as to the known conditions entirely. Proliferation proceeds from the rod-like motionless bodies, bacteria, which probably by progressive splittings in the long axis, give rise to " groups of isolated bacteria." By active division individual bacteria disappear, then arise " granular plasma-balls." Farther on there appears a differentiation of their contents ; a part becomes bacterian colonies, others remain homogeneous, have a dull and yellowish appearance, bear protoplasmic processes and appear contractile : " contractile pigment-bodies." The last stage consists in the formation of an homogeneous mass, in which are found neither pigment granules nor bacterian colo-

nies : " plasma-layer." From this the same development may proceed anew as from the first-introduced germs.

II. Group : Microbacteria :—rod-like bacteria.

Resemble globular bacteria in the small size of their cells, and their temporary union into jelly-like or mucous masses, but, apart from their physiological activity, they are distinguished by their short cylindrical form, and the spontaneous movement of their cells.

2. Genus.   Bacterium *sensu str.*   Cohn.

Short cylindrical or elliptical cells, which during segmentation are connected in pairs ; the daughter-cells separate after complete division ; rarely they again divide before they have become isolated, and then four cells are found in one row.   The cells enjoy a lively spontaneous motion through abundant nutritive supply and access of oxygen, so that times of rest are often succeeded suddenly by motion.   They do not form chains or filaments (thus do not appear in form of leptothrix or torula), but vegetate to form jelly-like masses (zooglöa-form), which are distinguished from those of globular bacteria by an abundant and permanent intermediate substance.

1. bacterium termo, Ehrenberg, Dujardin.

Cells short, cylindrical, oblong, clear glistening or blackish according to position, the membrane comparatively thick.   Mostly connected in progressive division or in pairs.   For the most part only 0,0015 mm. long, $\frac{1}{2}$—$\frac{1}{3}$ as broad.   They fill up water in countless myriads as soon as putrefaction matter is present, and increase as long as putrefaction goes on, and disappear as soon as it stops.   " Bact. termo is the ferment of putrefaction, the saprogenous ferment."

The cells turn on their long axis and swim forward, then return a little or travel in curved lines through the water, for the most part not very quickly, as if trembling or wavering, also shooting forward with sudden springs, then again becoming quiet for a long time.

2. bacterium lineola, Cohn.   (*Vibrio lineola*, Ehrb. Duj.).

Cells distinctly cylindrical, 0,0038 to 0,0052 mm. long, to 0,0015 mm. broad, straight, rarely somewhat curved, with strongly refractive, soft contents which are also abundantly filled with fat-like granules, and thereby darkly punctated.   They are single or connected in pairs.   They form zooglöa-form masses like *bact. termo.*

They move like b. termo, but more strongly, swim about one end tremblingly or in curved lines, alternately forward and backward, etc.

Klebs (l. c.) regards rod-bacteria as a phase of development of globular bacteria. He regards both as microbacteria with the following characters : cells colorless or feebly colored, very small, globular or oval (micrococcus), which unite into many-celled families (zooglöa).   Within the latter the micrococci grow into rod-shaped forms (bacteria), which become free and freely movable.

III. Group : desmobacteria :—filamentous bacteria.

Consist of elongated cylindrical parts, which if isolated, are similar to *b. lin.* but they increase by transverse division, and form by uniting, longer or shorter chains or filaments.   The filaments are not constricted at the joints, like the moniliform chains (torulaform) of the globular bacteria, but throughout cylindrical (leptothrix filaments).   They often form swarms, never zooglöa-form masses.   Their state of motion and rest changes with

the contained oxygen, etc.; certain forms appear never to be movable (*bacteridium*, DAV.).

3. Genus. BACILLUS.

Filaments straight.

1. BACILLUS SUBTILIS, COHN (*Vibrio subtilis*, EHR.), butyric-acid ferment.

Filaments very thin and tender, hence the articulation is seen with difficulty; the single articulations are mostly 0,006 mm. long, sometimes isolated (then distinguished with difficulty from *b. lineola*), sometimes made up of two articulations or forming still longer rows. Filaments in high degree supple, actively and passively.

They swim straight, with alternating rest, sometimes clumsily, sometimes quickly and dexterously, then back again without turning around. They turn continually about their axis. The filaments for the most part make visible pendulum like movements about a varying point in the length of the filament.

2. BACILLUS ANTHRACIS, bacteridia of gangrene of the spleen (DAVAINE).

Very similar to the preceding.

3. BACILLUS ULNA.

Filaments thicker and stiff, with dense finely granular plasma.

4. Genus. VIBRIO.

Filaments wavy: either thick with single curving (*vibrio rugula*), or thin with many wavy curves (*vibrio serpens*).

IV. GROUP: SPIROBACTERIA:—SCREW-BACTERIA.

They are distinguished from *vibrio*, COHN, by the closer and narrower, regular, permanent spiral of the filament. The various forms occur mostly in company together. They appear only in infusions for which river-water is employed.

5. Genus. SPIROCHÆTA, with a more flexible and longer closely-wound spiral.

SPIROCHÆTA PLICATILIS. In tartar from the teeth.

6. Genus. SPIRILLUM. With stiffer, shorter, and more distant spiral.

Spirillum tenue, spir. undula, spir. volutans.

A special arrangement includes the following plants: leptothrix and sarcina.

LEPTOTHRIX BUCCALIS.

Consists of long, very slender (0,0008 mm.) simple filaments which are divided by partition walls, and very brittle. In every one it occurs upon the finely granular masses of decomposition within the mouth (summit of the papillæ of the tongue, sediments around the teeth, tartar); in great masses in the sick, with thick brown coating on the tongue (typhus). Constant in the intestines, and in the feces. Very frequent in the vagina, sometimes in the lachrymal ducts. Without special local pathological significance, but the cause, perhaps, of caries of the teeth.

Most observers admit a filament formation in all bacteria without distinction; COHN does not. The chains of globular bacteria are distinguished from leptothrix-forms of filamentous bacteria by the fact that the latter are not constricted at the articulations.

According to L. MAYER (*Monatsschr. f. Geburtsk.*, XX., p. 2) and others, a similar parasite consisting of broad filaments occurs also in the normal and morbid secretions of the vulva and vagina. According to WINCKEL (*Berl. kl. Wochenschr.*, 1866, No. 23) the broad forms only rarely have in pregnant women any other results than, perhaps, hyperæmia and increased secretion.

A parasite resembling the *Leptomitus uteri* and *muci uterini* was found by L. MAYER (l. c.) upon the inner surface of the labia and in the vagina. It forms spots, whitish or

yellowish, as a rule, loosely distributed upon the mucous membrane, rounded or ir-
regularly formed, with a diameter of from 4 to 16 mm., resembling patches of thrush.
Sometimes they cover these great surfaces. Less often they adhere like diphtheritic
membranes to the mucous membrane, and when removed leave behind superficial
ulcers.

According to LEBER and ROTTENSTEIN (*Unters, üb, d. Caries der Zähne.*, 1867)
caries of the teeth depends upon the growth of *leptothrix buccalis*. In the interior of
the enlarged tubuli of the teeth granules of fungus are found, which can expand the
canals into broad pouches ; then originate processes filled with fungi, which procure
the resulting complete decay of the tooth. At the commencement of caries the
enamel and dentine are, by means of the spores (which originate preferably in the
mouth through various processes of fermentation), attacked in the same place, be-
come softened and thereby prepared for the entrance of the fungus. (According to
others, chemical substances, especially acids, destroy living as well as dead teeth.)

FÖRSTER (*Arch. f. Opth.*, XV., p. 318) and v. GRAEFE (*Ib.* p. 324) saw *leptothrix*
in the lachrymal ducts, and, as a result, stillicidium and catarrh of the lachrymal
ducts.

LEBER (*Med. Ctrlbl.*, 1873., No. 9) induced by inoculation of masses of lepto-
thrix (out of the normal oral cavity) upon the cornea of a rabbit, a very intense hy-
popyon-keratitis, similar to that of man : microscopically, a dense infiltration of pus,
but no fungus growth. The identity of LEBER's disease with EBERTH's diphtheritis
of the cornea is questionable. Probably, however, progressive suppurative keratitis
of man arises by septic infection, in many cases, perhaps, from the decomposing se-
cretions of the lachrymal passages, in diseases of these parts.

The following fungi are doubtful, having been found at the most only once or few
times : *Leptomitus urophilus* (RAYER); *Leptomitus Hannoveri ; Leptomitus epidermidis*
(GUBLER) ; *Leptomitus uteri* (LEBERT) ; *Leptomitus muci uterini* (WILKINSON) ;
Leptomitus oculi; Oscillaria intestini (FARRE).

SARCINA VENTRICULI, (GOODSIR) :—SARCINA. (*Merismopoedia punctata s.
ventriculi.*)

Forms 4, 8, 16, 64-(etc.) fold flat cubical cells with an average size of 0,01
mm., each of which is usually divided deeply into four parts and for the
most part contains 2 or 4 pale or slightly reddish nuclei : it is seldom with-
out nuclei. They lie together in cubical symmetrical heaps. Out of these
cells, rounded cells are at first formed through continuous quadruple stran-
gulation and division. The cells are heavier than water and sink in liquids.
It occurs especially in the fluids of the stomach (vomits), less often in
the fluids of the intestines (diarrhœic stools), in the urine, in pus, and fetid
liquids in various localities. It is probably for the most part without
pathological significance.

Whether the sarcinæ occurring in different localities belong to the same species is
not surely determined. According to ITSIGSOHN (*Virch. Arch.* XIII., p. 541) sarci-
na originates from some one of the *Oscillatoriæ*, several species of which occur in
our springs. According to WEISE (*Berl. kl. Wschr.*, 1870, No. 34), probably from
Diatomaciæ, and so is neither a true animal nor vegetable form. He proposes for it
the name of *Frustula ventriculi*.

According to COHN (l. c.) sarcina is a genus of the *schizomycetes ;* it divides cross-
wise by partitions, bacteria only traversely. COHN saw sarcinæ outside the human
organism on cooked potatoes, as did also LOSTORFER in the blood.

As *Pneumonomycosis sarcinica* VIRCHOW (*Arch.* IX. p. 574, X. p. 401) and
COHNHEIM (*Id.* XXXIII., p. 157) have described cases in which the sarcina was pro-
bably the cause of pulmonary gangrene. In other cases it had doubtless passed out
of the stomach into the lungs (ZENKER and others).

In what follows, we shall consider the vegetable parasites with respect
to their relations to the human body. Therein, on account of our
imperfect botanical and pathological knowledge, there exist manifold un-
certainties, and repetitions cannot be avoided.

1. The so-called mould-diseases, or mykoses.

The mould-diseases are conditional upon the above-mentioned mould-fungi. They are all called from their locality: Dermato-, Pneumono-, (etc.) mycosis aspergillina. They occur first of all only upon parts affected with necrosis, or other lesions, particularly upon ulcers of the skin (incl. the nails and external organs of hearing) and of mucous membranes, as well as in parenchymata with which these parts are more or less connected (lungs—expectoration). When found upon free surfaces and not too feebly developed, they present to the naked eye an appearance resembling mould: they form now sharply defined, circumscribed spots, now an irregular more diffuse covering of a dirty greenish grey color. When the mould happens upon the nails, before or after previous splitting of the body, a thickening appears, and a yellowish discoloration shining through from beneath, which sometimes occupies the whole length of the nail, sometimes only its anterior, and lateral portions.

Consult the collections of HEUSINGER (*Ber. d. Würzb. zoot. Anst.*, 1826) and VIRCHOW (*Arch.*, IX., p. 557). Since then numerous isolated observations of MYKOSIS occurring in several localities have been published: most relate to the external organs of hearing, (CRAMER, MAYER, SCHWARTZE, STEUDENER, WREDEN,) and the lungs (VIRCHOW, FRIEDERICH, DUSCH, COHNHEIM.)—Particularly numerous are the cases of mould formation within the healthy as well as diseased air-passages and air-chambers of the bones of birds. Upon the mucous membrane of the air-passages, this formation is sometimes so active that the entrance of the air into the lungs is hindered (GLUGE, and others).
SALISBURY (*Schm. Jb.* CXXI., p. 49) saw among threshers, and in military camps, an outbreak resembling measles caused by fungus spores from straw. [*Am. Jour. of Med. Sci.*, 1862, II., p. 17, p. 387.]
Perhaps here also belongs the so-called MADURA-FOOT (HIRSCH) or MYCETOMA (CARTER), of whose fungus very little is yet known. In isolated districts in the East Indies the complaint is endemic, occurring preferably on the foot, and causes, in the attacked part, considerable deformity and dull pain. The fungus grows first in the subcutaneous cellular tissue, which thereby and in consequence of the inflammatory infiltration is greatly thickened. For the most part only after several years' duration, warty nodes arise, which become perforated and emit a thin, yellowish, stinking liquid with numerous little black masses, which contain among other things, fungus-filaments and spores. The ulcer passes through the soft parts to the bones. Death results for the most part from marasmus. (Consult the descriptions, GILL and A. V. CARTER, BIDIE and the collections of cases by HIRSCH in *Virch. Arch.* XXVII., p. 98.)
In many cases, disorders of the digestive apparatus have been observed after the use of mouldy bread and sausage. With respect to this, indeed, it remains questionable, whether mould fungi or the chemical changes of the food are the cause of the affection (HUSEMANN, *Hdb. d. Toxicologie*, 1862. Suppl. 1867.). MOSLER (*Virch. Arch.* 1868, XLIII., p. 161) saw inflammation of the mucous membrane of the stomach arise through the use of blue milk (the blue color was due to fungi).

II. The fungi of the true parasitic diseases of the skin and mucous membranes.

The parasites under consideration come passively upon or within the body. They reach the outer surface through the air, or by direct or indirect contact (clothes, bedding, combs, razors, etc.). The infection is communicated sometimes from man to man, sometimes from domestic animals to man; especially often does the latter occur in the parasitic forms of herpes. These parasities happen upon the mucous membranes or within the body, even in the lymph and blood-vessels, through immediate accidental transportation (*e.g.*, in catheterization), or through the air which we inhale, or with the food.

The fungi indicate no special predisposition on the part of their bearer. They grow and increase as well probably upon the healthy as upon the sick. Moisture and warmth (damp dwellings, moist poultices, woollen under-garments), are particularly favorable.

The local maladies of the skin and of the mucous membranes, particularly those provided with laminated epithelium, have until now been almost the only ones fully known. Whether fungi attack the altogether normal portions of the skin and mucous membrane, and there develop, is still in dispute : usually indeed it is the portions of skin which were kept less clean, and of mucous membrane of the same kind, or such as had suffered impaired function, or where previously small erosions had existed. From such places, then, the fungous growth spreads about upon the surrounding normal structures. The filaments and spores grow and increase preferably between the epithelial cells (with most difficulty between those of the upper layer,—most easily between those of the middle layer), between which arise the hair and nails, causing them to become loose, and effecting their atrophy and final destruction or falling off. In this formation pus does not usually appear; but there exists for the most part a marked hyper-æmia. Growth takes place partly on the surface, often so that larger or smaller sharply defined groups arise, partly beneath the surface, with or without the aid of the gland-ducts of the hair, and the hair-follicles. In the deepest epithelial layers, on the surface of the fibrous tissue of the skin and mucous membrane, the growth of the fungi usually ends. Rarely do they grow between the fibres and pass into the vessels of the lymphatic and vascular systems.

The consequence of the presence of the fungi referred to are :

IRRITATION OF THE SENSORY NERVES, which results, partly perhaps in a direct manner from the presence of the fungi, between the epithelial cells, but in great part from hyperæmia, which the foreign bodies maintain by their spreading and growth. Thus arises the not infrequent violent itching in *pityriasis versicolor*, and the burning sensation of the mucous membrane of the mouth in thrush.

If the fungous deposit is considerable, it gives rise like other foreign bodies to INFLAMMATORY IRRITATION, which leads to erosion and ulceration (particularly the favus and thrush fungi). Thereby the neighboring lymphatic glands may become swollen.

By the pressure of the fungous masses, the subjacent skin undergoes ATROPHY, by their growth into the hair-follicles and hair, destruction and falling off of the hair follows, as in *herpes tonsurans* and in *favus*.

When the quantity of fungi is large, they cause, in addition to the CHEMICAL DECOMPOSITION OF THE CONTENTS OF THE CAVITIES which they in-habit, swelling, *e. g.*, as the thrush of the oval cavity. In this manner, new irritations can arise, which lead to convulsive muscular movements, vomiting, eructations, or to catarrhal secretion, to diarrhœa, etc.

Only by enormous growths of fungi do STRICTURE AND CLOSURE OF CHANNELS occur, such as, most rarely, of the œsophagus, and the great air-passages by the thrush-fungus.

In rare cases, where the fungi penetrate the bloodvessels, LOCAL THROMBO-SES, OR EMBOLIC MASSES of the fungus itself can perhaps occur with the usual consequences. (*Vide infra*.)

First of all, SCHÖNLEIN in 1839, for favus, and soon after J. VOGEL, for thrush, furnished exact proof that fungi were the cause of local disease of the skin. Very quickly then were fungi discovered to be the causes of other diseases of the skin and mucous membranes.

While the ætiological signification of these fungi has thus been determined, it has, in later years, on that account especially, been questioned whether the different fungi truly belong to different species, and whether most of them do not belong to the same mould-fungus. (T. Fox, Hallier.)

The fungi to be studied in this connection are:
TRICOPHYTON TONSURANS (GRUBY). This consists of round, transparent, large (0,044—0,01 mm.) spores or spore-rows. They develop in the roots of the hair and pass hence into the shaft of the hair, so that the latter is entirely destroyed and breaks off; likewise in the sheath of the hair-roots, and surrounding epidermis, seldom in the nails. This is the reason of the occurrence, especially upon the scalp, and more rarely on other parts of the skin, of *herpes tonsurans* (ringworm, *porrigo scutellata, teigne tondante, phyto-alopecia*); also of the parasitic forms occurring upon the beard, *mentagra* or *sycosis*, of *eczema marginatum ;* likewise, finally, of many forms of *onychomycosis*.

According to HALLIER (*Gährungsersch.*, 1869), the trichophyton proceeds from aspergillus. NEUMANN confirms HEBRA'S opinion founded on clinical observation, that herpes tonsurans and favus can arise by one fungus, and indeed, according to NEUMANN, from *penicillium*, in single cases also from *trichothecium*. In WYSS' (*Schweiz. Corr.-Bl.*, 1871, I., p. 45) experiments in cultivation with mycelia from herpes tonsurans and favus, there were developed, after three months, numerous fruit forms of *aspergillus*, for the most part of the usual appearance, in part also with filamentous greatly elongated basidians.

According to GERLACH, an affection similar to herpes tonsurans occurs in cattle (*Die Flechte des Rindes*, 1857) and in dogs (*Mag. f. Thierheilk.*, 1859), and according to STEIN (*Prag. Vjsc'r.*, 1860), and BÄRENSPRUNG (l. e.) an affection similar to h. circinatus occurs in cats. BÄRENSPRUNG (l. e., p. 124) furnishes a number of examples in which herpes circinatus and tonsurans were traced back to an infection emanating from domestic animals (cattle, horses, dogs, cats). OTTE, FRAZER, TUCKWELL, and others, have made similar observations.

In HERPES TONSURANS of the scalp, there appear one or more round bald spots of varying size, where the hair is entirely absent or broken off near the surface, and without lustre and elasticity. According to NEUMANN it appears:

(1.) As *h. tons. vesiculosus:* small punctiform vesicles with clear contents, arranged in circular form, which after a few hours dry, leaving behind small thin scales and crusts. Immediately after new vesicles arise with similar destiny, and thus peripherically the disease increases in extent.

(2.) *h. tons. maculosus* forms pale reddish spots, in the centre of which is a slight whitish scurf; they spread peripherically, while the centre grows pale, thereby giving rise to a form of *erythema annulare.*

(3.) *h. tons. squamosus*, a later stage of the two forms named above.

The cause of MENTAGRA, or SYCOSIS was formerly held to be a special form of fungus, the *microsporon mentagrophytes* (ROBIN). There are, however, according to KÖBNER (*Virch. Arch.* XVII., p. 372) and ZIEMSSEN (*Greifsw. Beitr.* II., p. 99), two forms of mentagra, one purely inflammatory (*folliculitis barbæ*), the other parasitic. The fungus of the latter is identical with that of herpes tonsurans. This is proven by the form, size, and propagation of the fungi, so that herpes tonsurans can be generated upon the skin of the same or of another individual by means of the crusts of sycosis, and in turn the crusts of h. tons. can give rise upon a healthy beard to a sycosis. The fungus, in sycosis, is developed between the hair and root sheath, grows from beneath the loosened hair and causes its atrophy, while the tissues surrounding the hair-follicle degenerate into a condylomatous swelling (papillary hypertrophy.) That the fungus causes more marked appearances in the skin of the beard than on the scalp, is accounted for by the more considerable size and deeper implantation of the hair-follicles, and by the thickness of the corium and subentaneous cellular tissue rich in glands and vessels.

The ECZEMA MARGINATUM of HEBRA, which is characterized by its constant localization on the inner surface of the thighs, on the mons veneris, and on the skin of the seat, much more seldom on other parts (in the beginning appearing as large, red, raised spots), by its peripheral advance and simultaneous involution in the centre, by the marked limit of the periphery in the form of a raised brownish-red border, upon

which scales, papules, and pustules, later sometimes also crusts, are often found, as well as by its almost exclusive occurrence in man, and especially in shoemakers, is, according to KÖBNER, dependent upon *trichophyton tonsurans* (or *microsporon furfur*, NEUMANN.) This is shown by the course of the disease, knowledge of the parasite, and experiment. According to NEUMANN, the fungus elements in eczema marginatum grow by cultivation into *penicillium glaucum*, or into *trichothecium*. In other cases *ecz. marg.* originates in an already preformed *ecz. intertrigo*, so that the fungi belonging to the latter grow on between the cells of the epidermis and then modify the form of the propagation of the eczema (NEUMANN).

ONYCHOMYCOSIS, in which one or more nails appear loosened and thickened, and have a dirty-yellow color, an uneven, fissured surface, and are easily split, is in many cases due to *trichophyton tonsurans*.

ACHORION SCHŒNLEINII : FAVUS-FUNGUS.

The mycelium consists of simple, or branched, cylindrical, curved filaments, which are either articulated or divided by partition walls. Of these are formed the long, broader, filamentous receptacula, which are articulate and contain rows of spores. The spores are round or oval ; send forth single or manifold shoots, and form jointed series of filaments, out of which the mycelium is developed. Besides, micrococcus continually appears. It is found in the deeper layers of the epidermis, later, also, in the sheaths of the hair-roots, and in the shafts of the hair themselves, although only between the cells. The size of the scabs is 1–10 ☐ mm., their thickness 1–6 mm., scutellate, yellow or brownish from dirt, dry and brittle, and they consist of an outer amorphous finely-granular mass, and an inner proper fungus-mass. The latter shows especially upon its exterior the mycelium, in the interior follow the receptacula, innermost are the spores.

This is the cause of FAVUS (*tinea* or *porrigo lupinosa, tinea favosa*) especially on the scalp, more seldom on other parts of the body, extremely rare on the whole body ; and of most forms of onychomycosis.

ZANDER saw favus also in cats and mice.

Those affected with favus incur the nail-fungus by scratching (KRAUSE, RIPPING, B. WAGNER, and others).

According to HALLIER (l. c.), STARK (*Jen. Ztschr.*, II., p., 220) and PICK (*Untersuch. üb. d. pflzl Hautparasiten*, 1865), special experiments by inoculation with *favus*, *herpes*, and *penicillium* (or *aspergillus*) all yield a similar result : (1) in epidermal inoculation of favus fungus, a herpetic eruption generally precedes the development of the favus crusts (initiative herpetic stage of KÖBNER) ; (2) this passes on to *favus*, or to *herpes tonsurans* ; (3) inoculation with fungi from *herp. tons.* generally yields again only *herp. tons.*, sometimes, however, a form of diseases is developed which is identical with the herpetic initiative stage of favus, and being abortive passes away ; (4) after a long duration of the favus, in cases of more luxurious vegetation, organs of fructification appear, which belong to the *penic. glauc.* and to a form of *aspergillus ;* (5) inoculation with *penic. glauc.* on the skin of man gives rise to a disease identical with initiative herpetic stage of *favus ;* (6) thus, one and the same fungus gives rise at one time to *favus*, at another time to *herp. tons. ;* (7) this fungus does not occur exclusively in diseases of the skin, but belongs in nature to a very widespread species of fungus.—STRUBE. KÖBNER (l. c.) and others, observed that *herp. tons.* always gave rise by inoculations only to *herp. tons.* and that only *favus* always arose by inoculation with *favus.* The herpetic initiative stage of *favus* is, according to K., indeed similar to *herp. tons.*, but not the same.

According to RINDFLEISCH (*Virch. Arch.*, LIV., p. 108) the identification of *achor. Sch.* with *penicillium, aspergillus*, etc., is premature ; rather achorion belongs to a place intermediate between yeast-fungus and thread-fungus, where articulate filaments and higher differences with respect to fruit-formation are opposed.

MICROSPORON AUDOUINI (GRUBY).

Consists of undulating forked filaments upon which small spores are directly placed. Found around the shaft of the hair, after its exit from the follicle, in masses so thick that the hair breaks off for the most part at that place and causes baldness.

It is, according to GRUBY, BAZIN, HEBRA, the cause of PORRIGO DECALVANS (*area Celsi s. alopecia circumscripta*), while according to HUTCHINSON, BÄRENSPRUNG, THE AUTHOR, RINDFLEISCH, KOHN, this affection is not parasitic, but of a nervous nature. *vide infra*.

MICROSPORON MINUTISSIMUM (BURGHARDT and BÄRENSPRUNG.)
Is distinguished by the special delicacy of its elements. It is the cause of a limited contagious affection, for the most part upon the inguinal, or axillary regions, the so-called ERYTHRASMA, which like the *pityriasis rubra* appears in the form of rounded or rosette-like, red, sharply defined dry spots KÖBNER saw several such cases.

MICROSPORON FURFUR (ROBIN).
Consists of masses of large (0,005 mm.) round, mostly nucleated spores and lengthened or branched cells, and only sometimes of very numerous broad (0,004 mm.) filaments. The spores shine, have a sharp double contour and form dense clustered groups. It is developed in the horny layer of the epidermis, commonly around the opening of the hair-follicles, especially upon the breast and back, never on the freely exposed parts of the body, nor on children. It causes yellowish or reddish-yellow, spotted discoloration of the skin, the spots covered with bran-like scales, and sometimes violent itching—it is the cause of PITYRIASIS VERSICOLOR, or CHLOASMA.

According to PAOLINI and GAMBERINI, a fungus similar to that of *favus* and *pityriasis versicolor* is also found in icthyosis.

ZOOGLÖA CAPILLORUM (MARTIN and BUHL).—Agrees mostly with the forms of *palmella*. Consists of a structureless, jelly-like basis-substance in which very small cells, analogous to the yeast fungi, are embedded. It colors the hair, first yellow, yellowish-red, blood-red, brownish-red, finally brown and even black. It is situated under the external layer of the hair. (*Ztschr. f. rat. Med.* 1862, XIV.)

OÏDIUM ALBICANS (ROBIN): THRUSH-FUNGUS.
Consists of cylindrical, branched, curved, strongly refracting, sometimes branched (tree-shaped) filaments, which are composed of long cells connected together, between which constrictions are often found. Each of the long cells contains many granules. The ends of the filaments are lost in masses of spores, with a large, often divided spore-cell. The free end is simple, rounded, or terminates in one or several large oval spores connected together. The latter are round or oval, often united to one another, contain granules and constitute large masses upon the epithelium. It is often found, and sometimes in large masses, in nursing children, especially within the first weeks of life, as well as in adults affected with wasting diseases (typhoid fever, tuberculosis, etc.): upon the mucous membrane of the mouth and throat, seldom upon that of the œsophagus, nose, large air-passages, lungs; seldom upon the labia, breast and lips of infants. It occurs in infants especially through want of cleanly attention to nursing-bottles, and in warm weather. It represents the so-called thrush, aphthæ. The aphthæ of the new-born form grayish or yellowish white round spots of the size of a pin-head or lentil, especially upon the boundary between the hard and soft palates. They gradually enlarge, unite and ulcerate. The aphthæ of adults are situated especially on the mucous membrane of the lips and cheeks and on the end of the tongue.

According to BURCHARDT (*Char. Ann.*, XII., p. 1) the fruit-capsules of the thrush-fungus present round or oval, sometimes double-contour capsules, .02 to .083 mm. in size, which are entirely filled with spores, and burst very easily. B. could not discover connection between the capsules and filaments.
In opposition to WINCKEL (s. p. 93) and in accordance with HAUSMANN (*Berl. med.*

Ctrbl. 1869), the fungus occurring on the female genitals is identical with *oïdium albicans*. It is like the latter, transmissible. Also the pure thrush-fungus of the mouth is transmissible to the vaginal mucous membrane. Sowings with *penic. glaucum, asperg. glaucus*, the fungus of *pityriasis versicolor*, were attended with negative results.

KOHN (*Sitz. d. Ges. d. Wien. Aerzte*, 29 Mai. 1871) found in many cases of *eczema impetiginosum faciei* (*impetigo contagiosa* of others) filamentous fungi, once also their organs of fructification. It is still questionable whether in *herpes iris* and *circinatus*, as well as in *erythema multiforme*, fungi are essential or accidental.

DIPLOSPORIUM FUSCUM (HALLIER).

Sometimes on diphtheritic membranes of the throat. Consists of extremely delicate, scaly and irregularly ramified articulated filaments. The long extended branches are, with quite regular alternation, covered with short, perpendicular lateral branches. The branches seldom remain vegetative; for the most part they very soon show at the end a small folliculous swelling, which very quickly enlarges and is defined from the extremity of their bearers as oval, double contour spores. The spores assume at the time of their maturation, a bright brown color.

III. FUNGI AS EXCITERS OF FERMENTATION AND PUTREFACTION, AND AS CAUSES OF CONTAGIOUS AND OTHER DISEASES.

The mould and yeast fungi, in rare cases also a few other fungi, which have already been mentioned, probably also a few other not well known, have, besides a local, a very important general significance. This depends upon the fact, that their germs, everywhere present in the air, are probably the most essential cause of the various fermentations taking place without and within the organism, as well as of the putrefaction of organic bodies. In both processes the extraordinarily active vegetative fungi take up as nourishment formed elements out of the affected substratum, and so decompose the substratum itself.

That fungi are the cause of several, more or less specific fermentations (acetic, alcoholic, lactic, butyric, &c.) is very probable. Fermentation is that peculiar process of decomposition which organic bodies, especially those non-nitrogenous, suffer when they come in contact with a ferment or with organisms acting as ferment (*e. g.* the decomposition of sugar into alcohol and carbonic acid by yeast). Also, for the appearance of fermentation there must be a proper temperature, water, and, for the most part, access of atmospheric air.

The importance and specific nature of fungi for fermentation has been especially shown through the works of PASTEUR. According to LIEBIG and recently HOPPE-SEYLER, fermentation does not depend upon fungus, but is purely chemical, a process dependent upon so-called contact-substances. (*Med.-Chem. unters.*, 1871, 4 H., p. 561.)

Those fermentations are of pathological interest which take place in the organism, and particularly in those cavities which are provided with a mucous membrane (stomach, bladder, etc.). The organisms which excite fermentation (yeast-fungus, mould-fungus, often also vibrios and bacteria) are introduced casually, by the food and drink, and by means of unclean instruments (catheter) into the interior of the body. They sometimes cause slight irritations, sometimes inflammation of the affected mucous membrane and of the parenchymatous organs connected therewith, *e. g.*, the kidneys. This is due partly to the increase of the fungi, partly to swarm-spores, also indirectly, perhaps, to the chemical changes induced by them.

Whether the yeast-fungus and the sarcina-fungus exert an injurious influence upon the mucous membrane affected, is not yet determined (*vide infra*).

Very likely, however, with respect to bacteria and mould-fungi which find an en-
trance into the bladder by means of unclean catheters, alkaline fermentation of the
urine may occur with consequent so-called parasitic cystitis, pyelitis and nephritis
(TRAUBE, *Berl. klin. Wochenschr.*, 1864, No. 2).   See also KLEBS, *Hdb. d. path.
Anat.*, 1870, I., p. 655.

The fungus-formations observed on the mucous membrane of the mouth and intes-
tinal canal have sometimes only a local importance, sometimes they give rise to
severe and fatal maladies.   Bacteria in the mouth, on the teeth, stimulate the nitro-
genous remains of food to putrefactive fermentation, and produce lactic acid from
sugar—they are the immediate cause of common caries (see p. 94).   The thrush-
fungus gives rise usually only to a light local disorder of the oral cavity (see p. 99).
This is, however, not always so.   ZALESKY (*Virch. Arch.*, XXXI., p. 426), saw
thrush also in many spots in the stomach and small intestines; the child had had
violent vomitings, later also diarrhœa.   I (*Jahrb. f. Kinderhlk.*, 1868, I., p. 58) saw
an extension of this fungus into the lumina of vessels of the mucous membrane
of the œsophagus.   ZENKER (*Jahresber. d. ges. f. Natur- u. Heilk. in Dresden*,
1861 62) found in an extended encephalitis, numerous small sharply circumscribed
points of pus, which could be lifted up with a needle, and under the microscope
shown to be little masses of fungus filaments enveloped in a thin layer of pus.   The
mucous membrane of the tongue and throat was covered with masses of thrush.

As HAY-FEVER VIBRIONES, HELMHOLTZ (BINZ, *Virch. Arch.*, XLVI., p. 100) de-
scribes little vibrio-shaped bodies, which are expelled in an attack of hay-fever only
during violent sneezing.   The usually isolated single articulations are 0,004 mm long
and contain four granules in a row, which are again closely united in pairs.   They
move upon the warm object-plate partly with a trembling motion, partly by darting
forward and backward.

Furthermore, fungi are the causes of decay as well as of putrefaction of
organic, especially nitrogenous bodies : in the latter, reduction, in the
former, oxidation takes place.   In both processes the corresponding fungi
occur : in the former, the so-called anäcrophytes, which do not need the
direct influences of the air (vibrios) ; in the latter, äerophytes : monads
and bacteria.   In decay an active oxidation goes on under the influence
of the fungi, whose products are water, carbonic acid, ammonia and
organic compounds, more simple than those which were originally present.
The greatest part of the organic bodies is thus destroyed, so that only a
comparatively small quantity is taken up by the fungus as nourishment.
In the same substratum the process of decomposition differs with the
fungus present.   Decay is arrested, even at a temperature suitable for
decomposition, if the bodies attacked are protected from the access of
fungus germs.   Putrefaction, according to more recent investigations, is in
the same manner dependent upon bacteria, as the various fermentations of
non-nitrogenous bodies upon yeast-fungi.   (See p. 86.)

Experiments made by SPALLANZANI, later by FR. SCHULZE, SCHWANN, HELM-
HOLTZ, SCHRÖDER, v. DUSCH, v. d. BROEK, especially by PASTEUR, show that
organic substances, left to themselves, easily enter into decomposition simultaneously
with the appearance of fungi, etc. ; but that these substances do not change, and
remain free from fungus formation, if they are exposed to a temperature which kills
the fungus-spores present in them, or if such air has access to them out of which the
organic germs have been removed (by being passed through sulphuric acid, or solu-
tion of potash, or over a red-hot surface, or filtered through disinfected cotton
filters, or dry animal membrane).   By placing a fluid very prone to decomposition in
an alembic with very narrow neck, which is open, but bent from one side to the
other or downward, so that the germs happening to be present in the air cannot
fall into the liquid but must remain in the neck, and by boiling the liquid a few
minutes and then letting the vessel remain open, the liquid will remain intact and
free from organisms.   Break off the neck, and appearances of decomposition will be
present in from 18 to 24 hours.   (DE BARY.)

Besides the influence of fungi in ordinary decay, it is shown in other similar pro-
cesses : in the putrefaction of eggs, of fruits—where the fungi penetrate for the
most part only through injured spots of the shell or keel.

According to COHN (*Schles. Ges. f. vaterl. Cult.* Sitz. v. 14 Feb., 1872), all putrefaction is attended by the development of bacteria; it begins if the appearance of the latter is permitted, progresses regularly as the latter increase; with the arrest of the putrefaction, the increase of bacteria is also arrested, which precipitate a pulverulent deposit, or in jelly-like masses (zooglöa), (like yeast in thoroughly fermented solutions of sugar). Bacteria are excitants of putrefaction (saprogenous), the mould-fungi and infusoria frequently developed in putrefying substances are only attendants of these (saprophilia). Infection with bacteria takes place not through the air (APPERT, SCHWANN, PASTEUR), but (B. SANDERSON) only through contact with unclean surfaces of bodies (skin, instruments), especially through the water, which always contains bacteria-germs, unless freshly distilled. According to C. the transfer of bacteria-germs through the air takes place at least with difficulty. Bacteria are normally developed and increase in every liquid which contains, besides ammonia or nitric acid, a body containing carbon, free from nitrogen. Since bacteria assimilate nitrogen in form of ammonia or nitric acid, their action in putrefaction seems to be to decompose albuminous compounds into ammonia, which is assimilated, and into other bodies, which appear as co-products of putrefaction. Putrefaction is the decomposition of albuminous compounds by bacteria in a similar manner as alcoholic fermentation is the decomposition of sugar by the yeast-fungus.

RINDFLEISCH (*Virch. Arch.* LIV., p. 396) distinguishes two forms of schizomycetes of putrefaction, *bacterium* and *micrococcus ;* the former is a constant, the latter a frequent attendant of the process of putrefaction. Without the access of bacterium the common stinking putrefaction does not appear, unless the conditions of putrefaction have been the most favorable. Decomposition without stink (as in still-born children) takes place without schizomycetes. The germs of bacteria are present in enormous quantity in all terrestrial moisture. The air usually contains, especially if it has been very rainy, very many fungus-spores, but no germs of bacteria. (RINDFLEISCH, l. c.)

In how far fungi are present in the various forms of gangrene, is not yet determined. In the greater number of cases, fungus formation is surely secondary.

General diseases, of which fungi must without doubt be regarded as causes, are in human pathology very little known. On the other hand we know of many vegetable and animal diseases which are with certainty the result of fungi. Among vegetable diseases belong the so-called brand, rust, etc., of our grains, the grape and potato disease ; among animal diseases some affections, occurring widely, of caterpillars, flies, etc., as well as gangrene of the spleen of mammals.

The infection of plants by parasitic fungi takes place only after the latter have sent adrift a germ-pouch. The germs either find their way into fissures of the plants receiving them, then pierce into the spaces found beneath and from there into the intercellular ducts ; or, as SCHACHT has shown, they penetrate by a sort of absorption or chemical solution through the cell-walls, forming sharply defined holes, and thus go far into the interior.—The grape-disease is due to *oidium Tuckeri* (MOHL, *Botan. Ztg.* 1852, p. 9 ; 1853, p. 585 ; 1854, p. 137), the potato-disease to *peronospora infestans* (DE BARY, *Die gegenwärtig herrsch. Kartoffelkrankheit,* 1861), etc.

The importance of parasitic fungi for the lower animals, which through them are destroyed by millions, singly or epidemically, was first shown in the so-called Muscardine of the silk-worm (BASSI, 1835). Equally noteworthy is the fungus of the house-fly (*entomophthora s. empusa muscæ*). At first, numerous little colorless cells arise, in an unknown manner, in the blood of the animal. These quickly grow to a considerable size, retain their spherical or egg shape, or grow into stretched pouches. The back part of the body of the flies swells out considerably, their motion becomes slow, and they die with peculiar stretching and crooking of the legs. Already before death the cells have extended into the interior, and bear cysts with blind extremities, which elongate and branch root-like, and supplant and consume both blood and intestines. In from eight to ten hours after death, the membrane between the segments of the body becomes pierced by the ends of the cysts above mentioned ; these stretch out and form on their extremity a large rounded spore, which may be thrown out to a distance of 3 cent. The dead fly soon thereafter becomes inclosed with a white dust. Healthy flies have hitherto failed to become infected by the spores.

De Bary has discovered four different forms of fungus during investigations of caterpillar epidemics: *botrytis bassiana*, *cordyceps militaris*, *isaria farinosa* and *strigosa*. He observed the germination of spores on the skin of animals, saw the penetration inward of the germ-pouches, their further development in the interior, and the formation of new fructifying fungus. He demonstrated that only few spores need come upon the surface of caterpillars and penetrate into the interior of the animals, in order to increase moderately and cause death. *Botrytis bassiana* is the cause of muscardine in the silk-worm; *cordyceps militaris* is found on the pupæ of the butterfly; *isaria farinosa* occurs on caterpillars which devastate the North-German pine-forests; *isaria strigosa* on the bodies of insects.

Consult Frey and Lebert, *Abh. d. naturh. Ges. zu Zürich.* Lebert, *Virch. Arch.*, XII., p. 144. De Bary, *Bot. Ztg.* 1867, p. 1; *Ib.* 1869, p. 585. Brefeld *Abh. d. naturh. Ges. zu Halle*, XII., p. 1.

Gangrene of the spleen, which on account of its transmissibility to man, and on account of its relationship to malignant pustule, has special interest for us, is produced by bacteridia, or filamentous bacteria, which by their rapid development in the blood not rarely act like ferments in a fatal manner. Upon inoculation the disease reaches even to the smallest blood-drops.

Gangrene of the spleen of animals is usually endemic or epidemic. It occurs primarily only in the herbivora (swine, beef, sheep, etc.), but is transmitted from these to the carnivora and man. It is found especially in malarial regions, under the conditions of moisture and high temperature of the external air.

Gangrene of the spleen occurs most frequently with carbuncle: *i. e.* a circumscribed inflammation of the external skin, sometimes also of the superficial mucous membranes with fibrino-purulent hæmorrhagic exudation, and mostly with its termination in gangrene. Much more rarely it is found in form of a more diffuse and further extended inflammation. In both cases there quickly appears severe general suffering, attended by a mostly fatal termination. Autopsy shows the blood dark, tenacious, reddening with difficulty, slowly coagulating, with extensive imbibition; the spleen is for the most part very large and soft; under the skin, between the muscles, and about the vessels are jelly-like yellow or reddish-yellow fibrino-purulent exudations. Putrefaction is rapid. More rarely than these localizations of gangrene of the spleen are found general affections: either so-called apoplectic or fulminating gangrene of the spleen, in which animals after great agitation fall down and usually are quickly destroyed; or the febrile gangrene of the spleen, when, under high fever with initial chill, great weakness, stupefaction, etc., death appears.

Gangrene of the spleen in man never arises spontaneously, but always by contagion with individuals, or parts affected by this disease. The contagiousness is in proportion to the severity and acuteness of the disease of the animal. If the spleen and blood are most infectious, less so probably are the hide, hair, etc., and still less so the products of these (leather, glue, wool). Yet these parts retain even in the dried state for months their ability to infect. All men are susceptible to the poison. Infection affects especially farmers, shepherds, tanners. In the summer months it occurs most frequently.

Gangrene of the spleen occurs in man generally in the same forms as in animals. The primary carbuncle is most frequent on the skin, especially in those parts of the body which are not at all, or only at times covered (face, neck, fore-arms and hands); their origin is due to demonstrable inoculation. Much rarer is the diffuse or crysipelatous form. Both forms show sometimes only the appearances of local trouble, sometimes are accompanied by fever, and lighter, or more severe and fatal general symptoms.

The constitutional disease, gangrene of the spleen, is much less accurately known. It is found sometimes simultaneously with (the primary) carbuncle, sometimes this appears only during the course of the disease (secondary carbuncle), sometimes, finally, it is absent. The disease runs its course sometimes in one or in a few days, most frequently in a week, rarely longer. It is characterized by severe febrile general symptoms (exhaustion, pain in muscles, and headache, gastric disturbances, often colics), which are followed by general weakness, distressing apnœa, etc., and with symptoms similar to those of asphyxial cholera, by death. Similar appearances are observed at the autopsy, as in animals.

In all these cases, in man and animals, *schizomycetes* appear to be the carriers of the disease. These bodies disappear with the complete putrefaction of the blood,

which distinguishes them from the corresponding infusoria. Therewith also ceases their power to infect. They enter the body probably with the drink. They are observed in the blood, first in from one to five hours after the first symptoms of gangrene of the spleen, increase then from hour to hour very considerably in quantity and accumulate in the capillaries. The blood shows the farther peculiarity, that the red corpuscles are glued together and swim in the serum like scattered islands.

DAVAINE (*Compt. rend. de. l'acad. d. sc.*, 1863, LVII., p. 220) first discovered the corpuscles of gangrene of the spleen, but considered them of no importance. POLLENDER (*Casp. Viljschr.* 1855) found them in the blood of dead animals, BRAUELL (*Virch. Arch.*, 1857, XI., p. 132, 1858, XIV., p. 432) a short time before death; the latter, however, neither regards them as bearers of the contagion, nor ascribes to them an ætiological, but only a prognostic signification. DELAFOND (*Die Blutkrankheit der Schafe u. s. w.*, Uebers., 1844. *Rec. de la. méd. vét'r.*, 1860, VIII., July, Sept.) regards them as organisms similar to algæ, and as the contagium of gangrene of the spleen: after the death of the animal the rod-like bodies grow, but vibrios appear first with the putrefaction of the blood in this disease, whilst the rods disappear. DAVAINE (*Mém. de. la. Soc. de. Biol.*, 1865, V., p. 193, etc.) then made farther investigations, and demonstrated the connection of the corpuscles with gangrene of the spleen by inoculation. Consult also the general treatise of VIRCHOW (*Hdb. d. spec. Path.*, 1855, II., 1, Abth., p. 387) and KORÁNYI (PITHA-BILLR., *Hdb. d. Chir.* 1870, I., 2., Abth., p. 149).

BOLLINGER (*Med. Ctrlbl.*, 1872., No. 27) has lately made clinical investigations in the ox and horse, as well as experiments by inoculation. He found the corpuscles mentioned in the blood of animals affected with gangrene of the spleen, almost constant during life and after death. True gangrene of the spleen may be produced by inoculation with the blood of anthrax without these little rods, and yet the blood of inoculated animals contains these forms, because in the former (blood of anthrax) are found the germs of bacteria. And, *vice versa*, anthrax may be produced by inoculation with the blood of this disease containing bacteria, without the blood of the inoculated animal showing rod-shaped bacteria: it contains germs of bacteria, which may be developed *post mortem* into little rod-shaped bodies. The chemical action of bacteria of gangrene of the spleen in the living body depends, according to B., essentially upon the fact that they, on account of their enormous chemical affinity for oxygen, absorb it with great greed and in great quanity, whilst they withdraw it from the blood-corpuscles. Thus with the enormous number of bacteria, there is sometimes want of oxygen and an excess of carbonic acid: dyspnœa, clonic convulsions, dilatation of the pupils, sinking of the temperature, and finally asphyxia. Thus in the cadaver are found all the changes which result from poisoning by carbonic acid. The fulminant (apoplectiform) forms of anthrax are on that account to be ranged in line with cases of death from poisoning by prussic acid.

DAVAINE found bacteridia also in two examples of malignant pustule in men, who had died on the third day of the disease. Here they were found in the centre of the pustules between the epithelial cells in very large groups, in the middle of which they were crowded; in the periphery they lay in separate groups, between which were found the epithelial cells. From here they penetrated into the blood and lymph-vessels of the skin. Others afterward looked for them in vain in similar cases.

Many remarkable fatal cases, which have been observed in late years, are with the greatest probability related to gangrene of the spleen, and are certainly dependent upon bacteria: the so-called MYCOSIS INTESTINALIS. Its essential condition consists in the occurrence of great numbers of vibrios and bacteria in the blood; in a resulting, mostly circumscribed hæmor-rhagico-purulent inflammation of the mucous, or, at the same time, of the sub-mucous coats of the stomach or intestines, or of both, with very abundant schizomycetes, and in consecutive affections of the lymphatic vessels and glands belonging to these organs; in various affections, inflammatory or hæmorrhagic, of different organs, dependent upon the same fungi. The disease always ran a very acute course. The symptoms were not very characteristic: they belonged for the most part to the stomach and intestines; usually high fever and severe brain-symptoms. The termination was always fatal.

The first, yet not clear cases of this intestinal mycosis were recorded by WAHL-VIRCHOW (*Arch.* 1861, XXI., p. 579), and v. RECKLINGHAUSEN (*Ib.* 1864, XXX., p. 366). Then follows the important observations of BUHL (*Ztschr. f. Biol.*, 1871, VI., p. 129). These were complemented by the cases by WALDEYER (*Virch. Arch.*, 1871, LII., p. 541) and by the author. (*Ein Fall von tödtlicher Pilzkrankheit, Mycosis intestinalis. Festschrift,* 1872.) Consult also NEYDING (*Vtljschr. f. ger. Med.*, 1869, X. p. 241) and MÜNCH (*Med. Ctrlbl.*, 1871, No. 51).

In the same way as in the affections above mentioned, the mode of origin of other diseases is not yet proven. Many acute infectious diseases especially, which are certainly or probably contagious, have had their origin traced back to bacteria. The grounds adduced for this are partly theoretical, partly that the fungi have been actually found in the diseases in question. Among the theoretical grounds the most weighty are: the similarity of many of these diseases to those above described of plants and animals, especially gangrene of the spleen and *mycosis intestinalis ;* the course of many epidemico-contagious diseases in individual cases, and with respect to epidemics as a whole (similarity with respect to the periodical coming, spread, and disappearance of many lower organisms); the infectiousness of substances which have been evacuated by the sick, for the most part only after a certain time; the lapse of a fixed time between the moment of infection and the beginning of the symptoms of disease (as if essential disturbances appeared only after an increase of the fungus-spores taken up in the infection).

Among diseases in which fungi have been found during life (in many exudations of the throat, etc., in intestinal evacuations, etc.) or in the dead body, or where there has been a successful inoculation, belong diphtheria, pyæmia of puerperal fever, small-pox. In many of these diseases infection takes place through wounds, etc. (see Pyæmia), in others probably through the inspired air, or by food and drinks, especially drinking-water. Bacteria appear free or inclosed within white blood-corpuscles in the blood, and therewith into various tissues. They finally disappear in an unknown manner or are excreted with the urine, unless death sooner occurs. According to different observers, bacteria vary in different diseases (gangrene of the spleen, diphtheria, pyæmia): they belong collectively to the immovable globular bacteria. Besides, bacteria are probably not individually injurious, but taken into the bloodvessels they cause a decomposition of the blood, and give rise to poisonous secondary products.

Most numerous investigations concerning the parasitic nature of these diseases have been made in epidemic diphtheria of the throat: TOMMASI-HUETER, BUHL, OERTEL, TRENDELENBURG, NASILOFF. Here are found micrococci and bacteria for the most part in endless quantity, not only in the epithelium of the throat, in the young exudation cells, etc., but also in the mucous membrane, sub-mucous tissue, in the lymphatic vessels and glands which belong to them, in the blood, and farther in the lungs, kidneys, in the urine, in the spleen, etc. Diphtheria has been conveyed to rabbits by introducing diphtheritic masses into the opened trachea (TRENDELEN-BURG, OERTEL). After inoculations of diphtheritic membranes under the skin and into the muscles of rabbits, there arises an altogether specific process, which is distinguished from that arising after similar inoculations of pyæmic pus, gangrenous tissue, putrefying substances, etc. ; the organs and the blood in the former contain milliards of micrococci, etc. ; in the latter none (OERTEL). Substances from animals subjected to the former inoculations introduced into the air-passages of other rabbits, again cause diphtheria of these passages (OERTEL). Micrococci reach the interior of cells either by perforating the cell-membrane, or the hyaline plasma-cells surround the cocci and inclose them within themselves. They then take up the nitrogenous nutritive substance into themselves, so that a cell is consumed in twenty-four hours as far as the cell-membrane; they separate and quickly increase (*vide infra*, diphtheritic exudation).

HUETER (*Med. Centralbl.*, 1868, Nos. 12, 34, 35 ; *D. Ztschr. f. Chir.*, 1872, I., p. 91, etc.) has demonstrated, as if experimentally, in the sick, that monads (*aërobia*) developing in great number in putrefying blood, penetrate very largely into living tissues and into the circulating blood, even hence they may appear in the secretions of the body, and by their extent give rise to inflammatory processes of special kinds, especially diphtheria, erysipelas of wounds, so-called diphtheritic phlegmon. Besides, monads exciting putrefaction may penetrate through the vessel-walls into venous thrombi and thus give rise to putrefaction, emboli, and to metastatie inflammations.

According to KLEBS (*Beitr. zur pathol. Anat. d. Schussw.*, 1872, etc.) the deleterious character of pus, as well as the general infection (pyæmia) appearing during sup-puration, is dependent upon the presence of schizomycetes (KLEBS' *microsporon septicum*). These grow on the surface of wounds, penetrate into the tissues, induce decay, and reach the blood by perforation of the vessel-walls. They are the causes of secondary inflammations and suppurations. KL. confirms these statements also by experiment. He injected animals with fluids containing fungi, which often caused very widely-extended suppurations, and until death continual fever. The same fluids filtered through a clay cylinder did not induce suppuration, but high fever, which in one to three days passed away. (See, in opposition, WOLFF, *infra*.)

According to KLEBS (*Tagebl. d. Nat. Vers.*, 1872, p. 212) the development of the micrococcus does not take place in the blood of normal animals under conditions in which the blood of animals infected with microeoccus shows a great development of these. The distribution of micrococci in sepsis, variola, and rinderpest offers dif-ferences so characteristic, that a specific difference between them must be assumed. (KLEBS).

RINDFLEISCH (*Lehrb. der path. Gewebel.*, 1871, p 204) had already shown that the small abcesses of the heart in pyæmia, puerperal fever, etc., consist only of vibrios.

The subcutaneous injections of KLEBS, according to which only the fungus masses cause local suppurations and until death continued fever, the filtrate, on the other hand, only transient fever and never local suppuration, afforded in the hands of WOLFF (*Berl. Ctrlbl.*, 1873, Nos. 8, 9) other results : he found in rabbits only a gradual difference between the action of the filtrate and that of the fungus-holding sediment.

According to EBERTH's (*Med. Centralbl.*, 1873, No. 8) numerous experiments, the skin of the rabbit becomes diphtheritic by inoculation of the diphtheritic layer from the throat, of the endocardial deposits in primary malignant endocarditis, of the diphtheritic layer from the mouth, of the pus of inflamed veins, of those of pyæmia, of purulo-eronpous exudation in puerperal peritonitis, and of the blood in sepsis and diphtheria of dead lying-in women. According to E. pyæmia is mostly a diphtheria. Many forms of septico-pyæmia are compound mycoses of the bacteria of diphthe-ria and putrefaction. Farther experiments established a quantitative difference in the effect of bacteria of diphtheria, and those of putrefaction (on rotten flesh, in putrid urine and blood) ; they make probable the difference of these organisms.

Consult also the earlier observations of VIRCHOW (*Ges. Abh.* 1856, p. 709) and BECKMANN (*Virch.* Arch. XI., p. 64), the manifold researches of COZE and FELTZ (*Rech. clin. et expér. sur les mal. infectieuses*, 1872).

ORTH (*Arch. der Heilk.*, 1872, XIII., p. 265) describes a case of septic mycosis in a new-born infant whose mother had puerperal fever.

WALDEYER (*Arch. f. Gynäk.*, 1872, III., p. 293) found abundant bacteria in the diphtheritic deposits on the inner surface of the puerperal uterus, in the puriform masses of the lymphatics of the uterus and its connections, in the peritoneal, once also in the pleural and pericardial exudations.

HIRSCHFELD (*Arch. d. Heilk.*, 1872, XIII., p. 489), in numerous cases of fatal puerperal fever, found micrococci free, or in colonies on the puerperal ulcers, in the surrounding epithelium, in the submucous tissue, in the lymphatics, in the pelvic cellular tissue, in the exudation of serous cavities, in the pelvic lymph-glands, in the spleen, etc. According to his experiments the white blood-corpuscles take up the micrococci in great numbers upon the introduction into the blood of moderate quanti-ties of liquid containing micrococci. The spleen retains a part of them in its pulp-cells, and when they are abundant there appears a distinct swelling of the organ. Thus is explained according to H. the constant occurrence of acute tumor of the spleen in the diseases in question.

RECKLINGHAUSEN (*Vortrag in d. Würzb. phys.—med. Ges.* v. 10 Juni 1871) found in a whole series of infectious diseases, above all pyæmia and puerperal fever, besides typhoid fever, acute rheumatism of the joints, infiltration of urine and pul-monary gangrene, as causes of the multiple metastatic foci, with absence of a simulta-neous endocarditis, miliary accumulations of small organisms, which he regarded as

microcoei. R. found deposits of fungus in the kidneys especially frequent, sometimes still quite fresh without any reactive appearance, more often surrounded by a hæmorrhagic zone or purulent infiltrated tissue. They are found not only in the bloodvessels, especially the smallest veins, but also within Bowman's capsules and urinary tubuli, where they floated away with the urine, as was shown in the contents of the bladder either during life or after death. The filling up of those different channels is often so great, that knot-like swellings arise, which go on to perforation and escape of the fungus masses.

A fungus-form altogether different from the micrococcus, which consisted of knotty rods of green color, was discovered by R. in a case of scarlet fever, as elements of similar small foci in the renal pyramids. The urine of the sick person, who died on the sixth day, contained casts covered by the same elements. R. regards these metastases of fungus not as emboli in the sense adopted by VIRCHOW. The contrary is shown by the frequent extravascular position of the misplaced material (R. found micrococci also within the pulmonary alveoli), and by the absence of endocarditis.

WEIGERT (*Med. Centralbl.*, 1871. No. 39) found in the pocks of the dead body, which were most developed on the sixth day after the appearance of the first sign of the exanthem which further, at least in part, had an hæmorrhagic character, bacteria of the smallest form. They lay in pouches, which perhaps corresponded to the lymphatics; especially in the vicinity of the pocks. The same was seen in the small cutaneous hæmorrhages, which are found in decided hæmorrhagic cases without or with indistinct pock-formation.

According to KLEBS (*Arch. für exper. Pathol.* I., p. 31), giant-cells occur in the epidermis in variola, which cells are developed from the micrococci in the cells of the animal exciting the disease. They contain sometimes many, sometimes no nuclei.

F. COHN (*Virch. Arch.* 1872, LV., p. 239), likewise KEBER and others, have demonstrated in the liquid of the vaccine and variola pustule living unicellular organisms of the group of the so-called globular bacteria (*microsphæra*, family of the Schizomycetes); they are constantly present, and in the greatest number, and increase with extraordinary quickness.

POPOFF (*Wien. med. Jahrb.* 1872, p. 414) found the micrococcus once in putrid bronchitis, where the large and small bronchi, and especially the alveoli, were almost entirely filled by it; likewise once in diphtheria of the larynx; once in variola hæmorrhagica in the capillaries and pulmonary alveoli; twice in pulmonary gangrene.

WALDEYER (*Schles. Ges. f. vaterländ. Cult.* 4, Aug. 1871) saw colonies of bacteria in the liver, stomach, pancreas, supra-renal capsules, where they appeared as black spots of the size of a grain of sand, in a case of acute diffuse hepatitis. Also many hundreds of miliary foci of bacteria in the flesh of the heart in pyæmia. Bacteria were the sole cause in four cases of miliary abscess-like foci of the kidneys. W. saw also many cases of hæmorrhagic nephro-pyelitis in various acute infectious diseases, where in the mucous membrane of the renal pelvis, as well as in the bloodvessels interstitially, colonies of bacteria were found.

HALLIER and others found in the diseases in question, numberless micrococci in the blood, which by cultivation have germinated and passed into known fungi (measles : *mucor mucedo ;* typhoid fever : *rhizopus nigricans ;* variola : *eurotium herbarum,* etc.). LETZERICH affirms the same of whooping-cough. KLEBS (*Verh. d. Würzb. Ges., Jan.,* 1873) describes a micrococcus in measles.

ORTH (*Tagebl. d. Naturf.-Vers.,* 1872, p. 214) investigated traumatic erysipelas pathologico-anatomically and experimentally. He found in the fluid of this affection, besides various numerous red and white blood-corpuscles, enormous masses of bacteria. These were for the most part oval, in part also rod-shaped. They were absent in internal organs. According to ORTH (*Arch. f. exp. Path.*, 1873, I., p. 81) epidemic erysipelas owes its origin to a poison contained in the blood, as well as especially in the affected parts of the skin. It may be communicated to other individuals by inoculation with these fluids. Bacteria go hand in hand with the development of erysipelas. The characteristic symptoms of disease may be produced also by bacteria, which have been artificially cultivated. Bacteria are, however, only the indirect causes of disease, since they are not found in great quantity in the blood of those infected, and since their destruction lessens the activity of the infectious fluids, but does not wholly destroy it. They belong probably to the globular bacteria.

GREVELER and HÜTER (*Med. Ctrlbl.*, 1872, No. 49) investigated the general disturbances of the circulation after infection of frog by fluids containing monads. The white blood-corpuscles adhered in great number to the inner wall of the bloodvessels; but only a few wandered out. A remarkably great number of capillaries were excluded from the circulation; this is frequently caused by one or two white

blood-globules becoming adherent at the point of exit of the capillaries. Slow and incomplete circulation was found in other capillaries.

OBERMEIER (*Med. Centralbl.*, 1873, No. 10) found in remittent fever during the hot stage (not in the remission, and shortly before and during the crisis) very fine filamentous forms, which possessed a very rapid movement : the movement consisted partly of undulations in the filament itself, partly in curvings, cork-screw-like, etc.

Cholera also belongs among those diseases in which genesis of fungus is always brought forward anew. After the older English data (TWAYNE and BRITTAN, WILLIAMS and others) had been shown in part to depend upon gross microscopical illusions, the more recent ones of KLOB, THOMÉ and HALLIER met with a similar fate. In diarrhœas of every kind, also after laxatives (sulphate of magnesia : KYBER), in dysentery (BASCH) the lower vegetable organisms are greatly increased. VIRCHOW (*Arch.* XLVII. p. 524) found the same in a case of very acute arsenic-poisoning. As little demonstrated are the fungi of intermittent fever (SALISBURY, and others). How easily, even the most expert histologists fall into gross errors, is shown by the strife just ended over the corpuscle of syphilis (STRICKER, LOSTORFER.)

In the foregoing are the most important affections, which according to many are certainly caused by fungi, according to others only possibly, and which also have been the source of some doubtless erroneous views. Therein also has inoculation often been made mention of as proof with respect to pathogenesis. That in this the greatest precaution with respect to the kind of material to be inoculated, the performance of the inoculation itself, finally the critical examination of the result is necessary, is at once understood. But, especially with respect to the first and most important point, there have been the most frequent mistakes ; a preliminary clear representation of the elements of the question is yet wholly impossible. The so-called cultivations are wanting in most directions in certainty. Even the best botanists after investigating for years those fungi which are of the greatest importance for human pathology, determine only the so-called " physiological " and pathological species. Finally, it is conspicuous, that until now no two observers have, concerning the same disease, reached the same results : the specific fungus of one is disavowed by another, etc. But, in spite of all that, much is yet to be expected from the farther cultivation of this field, with respect to the ætiology, etc., of many diseases.

GROHE (*Greifsw. med. Sitzungsber*,1869) saw death appear 30-36 hours after injection of 2-3 C cent. of spore-fluid into the jugular of rabbits. At the autopsy fresh miliary tubercles or nodular abscesses, which consisted of fungi, were found in the lungs, heart, liver, kidneys, mucous membrane of the digestive tract, and muscles of the body. By injection of the same substance into the carotid, numerous fungus-foci were found in the substance of the brain, vitreous, &c. The fungi develop within the blood-channels, their ramification at first follows the course of the blood-vessels ; farther on they penetrate through the vessel-walls and develop further in the parenchyma of the organs. G. calls the process *mycosis generalis acutissima, s. foudroyante.* By injection of the spore-fluid into the abdominal cavity there were developed first on the peritoneum and its folds, common and mycotic tubercle : afterwards also in the liver, kidneys, less in the lungs and muscles.—Consult also BLOCK., *Beitr. z. Kenntniss. d. Pilzbildung in den Geweben des thier. Organ.*, Stettin, 1870.

SEMMER (*Virch. Arch.*, L., p. 158), in two series of experiments, injected into the blood smaller or larger masses of spores and yeast of *penicillium glaucum*, without important consequences. The same thing was shown, when in addition micrococcus or arthrococcus yeast was injected But, in a case in which gangrene of the spleen again appeared from infection by fungus spores and micrococcus which had been cultivated from the blood of the same disease, the outbreak occurred on the ninth day after injection, and the full development on the tenth day caused death.

[Consult also: DAVAINE, *Acad. de Méd. de Paris, séance du 28 Janvier*, 1873. Debate on the Germ Theory of Disease in the Pathological Soc. of London, in *Lancet*, April and May, 1875—ED.]

Numerous other researches are not given here, partly because of deficient

botanical knowledge, partly because of the frivolous comparison of fungus diseases with certain affections of man.

B. ANIMAL PARASITES: ZOOPARASITES.

Animal parasites inhabit either the outer coverings only (ectoparasites, epizoa), or only internal organs (entoparasites, entozoa); but this distinction is not strict.

The most frequent locations of animal parasites are the skin and intestines, nevertheless almost every organ harbors parasites. Many parasites live only in certain organs (*e. g.*, the encysted Trichina, the Strongylus gigas); others are found in different organs (*e. g.*, Cysticercus and Echinococcus). Many parasites are found only in man (*e. g.*, Pediculus capitis, Bothriocephalus latus); others are found in man and animals (*e. g.*, Trichina, Distoma hepaticum); but very seldom in several classes of animals (*e. g.*, Trichina).

The natural history of many parasites is almost entirely unknown, while we possess the fullest knowledge of the origin and development of others.

In general, the characteristic periods of the life of the entozoa are three, for the most part stages of development formally different from one another: the embryo, the intermediate state, and the mature animal. The embryo destined to produce the parasitic state remains mostly passive; the intermediate state takes up the process of development and carries it on so far that immediately after passing into the third stage maturity appears. The life of parasites is distributed, dependent upon two, and even more bearers, of which one harbors the young, the other the mature animal. These bearers are sometimes only individually different from one another, as in the case of trichina; more often they belong not only to different species and genera, but even to different orders or classes. The early states of individual entozoa are found especially in those animals which serve as food to the bearers of the perfected parasite (*e. g.*, the perfected Tænia crassicollis lives in the intestines of the cat; the young form, the Cysticercus fasciolaris, in the liver of mice. Tænia solium exists in its youth in swine, &c.

The fate of entozoa depends more upon chance than that of any other animals: the ovum must find its proper bearer, and the latter must, later and at the right time, be eaten by another and proper animal. Indeed, the more complex the life of a parasite is, so much smaller is the probability of its prosperity. In the case of the tape-worm, out of eighty-five millions of eggs only one is developed again into a tape-worm. Only the enormous fertility of parasites counterbalances this loss.

The immigration of external parasites upon and into the human organism is mostly an active one, that of internal parasites mostly a passive one. The most frequent and constant source of the latter is the accidental introduction of ova and the young.

Special attention is due to self-infection, *e. g.*, in Tænia solium (never the case with Tænia mediocanellata), the worms may directly change their abode from the intestine into the stomach, or by entrance into the latter through the mouth.

The DISPOSITION TO HELMINTHIASIS is a general one; age, sex, and nationality make a difference only because of incidental circumstances. The frequency of worms is limited above all by the opportunity of importation,

in which custom, habits, employment, and manner of living exert an important influence.

Jews and Mohammedans are seldom affected with tape-worm, because they do not eat pork. Butchers, cooks, and domestics have more frequent opportunity for infection with tænia and trichina. Children and the insane have thread-worms and round-worms more frequently than adults. Uncleanliness influences a change of place less than the fixation of the skin-parasites.

Thus is explained the dependence of certain forms of helminthiasis upon circumstances of time and place.

The thread-worm comes under the physician's care most often in autumn ; the tape-worm oftener in summer ; the *filaria medinensis* most often during the rainy season. Intestinal worms are most frequent in people living in a natural state in tropical and other countries. Every native Abyssinian, from six or seven years of age has a tænia. Most East-Indian negroes and most Hindoos have thread-worms. In North Germany, which is noted for its swine breeding, tape-worm is oftener found than in the South. Those Icelanders who live closely with their dogs often have the echinococcus.

The geographical distribution of animal parasites depends principally upon that of the intermediate carriers, from which man receives these parasites.

Animal parasites affect the human organism injuriously in a threefold manner.

They TAKE MATERIAL FOR NOURISHMENT FROM THE ORGANISM—of itself seldom of very considerable moment. Skin-parasites and tape-worms seldom act in this way, the thread-worms only by their great numbers; then arise signs of anæmia and nervous symptoms. But the *anchylostomum duodenale* causes through the blood which it wants for its nourishment, still more, however, through the hæmorrhage following its bites, the so-called Egyptian chlorosis, etc.

Far more important are the MECHANICAL INJURIES due to parasites. Larger parasites, as well as numerous small ones, lying in heaps, cause pressure and, finally, atrophy of the neighboring tissues ; thus cysticerci in several localities, e. g., the brain and the eye, echinococcus in the liver, etc. ; trichina in the muscles. In consequence of pressure, or, at the same time, of atrophy, sometimes no disturbances of function arise (e. g., in the not too numerous cysticerci and trichinæ of the muscles), sometimes those arise which, with regard to the position of the affected part respecting the whole organism, are of various importance ; by means of cysticerci in the brain, sometimes convulsions, sometimes palsies, sometimes mental disturbances arise ; through those in the eye-ball, blindness; through echinococcus of the liver, suppression of the specific function of the organ; through large numbers of trichinæ in the muscles, inability to move, etc. Farther on, there may arise secondary disturbances of the circulation, inflammations (e. g., of the serous membranes), pus-formations in the neighboring tissues, ruptures, sometimes with the contents passing into the intestines, or outward, particularly through the abdominal walls, etc., especially with the echinococcus. The parasites in the canals contract their calibre; acute stenosis of the intestinal canal may arise in consequence of numerous coiled thread-worms ; icterus, in consequence of the thread-worm in the larger gall-ducts. They give rise to catarrh and hæmorrhage, perhaps even to ulceration of the affected mucous membrane (tænia, thread-worms, etc.) ; thereupon arise disorders of digestion, with maladies both local and general.

Finally, the parasites ACT INJURIOUSLY BY THEIR MOTION AND MIGRATION, and thus cause sometimes pains of various kinds, such as pains in the muscles, itching of the skin, colics, the latter particularly in the fasting state, which directly or by reflex action, may give rise to farther trouble (itch-mite, tape-worms, oxyuris); sometimes perforation and rupture of the inhabited organs (echinococcus, perhaps also thread-worms).

All these conditions are only partly known with respect to man, but are well established through experiments on animals. They are best known concerning the itch-mite and trichina.

The SYMPTOMS OF PARASITES are in only a few cases (itch-mite, trichina) so characteristic, that it is safe to make a diagnosis from them. In most cases the demonstration must be objective. In these it is furnished either by the examination of the excreta, especially of the stools, sometimes of animals which have come away entire (thread and round worms, trichina), sometimes of articulations (tape-worms) or ova (thread and round worms, *bothriocephalus latus*), or by the examination of the skin (itch-mite), with the assisted eye if necessary, of the eye (cysticercus), or by examination after previous operations for obtaining the parasite (trichina, cysticercus), or less certainly by palpitation and percussion (echinococcus).

(In the following special consideration of parasities, use has been made of CLAUS, *Grdz. d. Zool.*, 1866, and LEUCKART'S work on Parasites).

1. PROTOZOA.

Creatures of small size and simple construction, without separate cellular organs and tissues, on the limits of animal life, with preponderating asexual propagation.

In the most simple instance, the whole body is a little mass of formless albuminoid substance, so-called SARCODE, whose contractility is limited by no outer firm membrane, which sometimes sends out easily fused projections, which when formed, are drawn in again; sometimes, with more glutinous consistency of the parts, it sends out a number of hair-like radiations and filaments—AMŒBA. Nourishment takes place by the gradual enfolding or pressing in of foreign bodies at any point of the periphery.

1. CLASS: RHIZOPODA.

Protozoa without enveloping membrane, whose parenchyma sends forth processes (pseudopodia) and draws them in; generally possessing a secretitious calcareous covering or siliceous framework.

FORAMINIFERA.

Rhizopoda which are partly naked, partly provided with shells which consist almost entirely of chalk, and for the most part are pierced at the egress of the pseudopodia by fine pores.

A number of organisms belonging to this class are, according to others, of vegetable nature—*e. g. amœba diffluens, arcella, difflugia*, etc.

2. CLASS: INFUSORIA.

Protozoa of determined form with an exterior (*cuticula*) covered with cilia, with a mouth and pulsating vacuola (*i. e.*, clear, mostly round cavities, filled with liquid, which contract and then disappear, but gradually become visible again, and enlarge to their original size, and which are mostly connected with vessel-like lacunæ); with male and female sexual organs, but, mostly asexual, propagating by gemmation and fission.

FAMILY : HETEROTRICHA. The body, over its whole surface, is thickly covered with cilia, which are often arranged in longitudinal rows. Besides about the mouth, is a surrounding zone of stronger cilia (STEIN).

BALANTIDIUM. On the left side of the longitudinal axis of the oval body is a buccal aperture provided with longer cilia.

BALANTIDIUM COLI, (MALMSTEN.) Very common parasite of the rectum of hogs, a few times found in the large intestine of man.

As PSOROSPERMIÆ are distinguished four different forms of animal parasites, which in the body of their host may, by their enormous accumulations, induce morbid conditions : 1. psorospermiæ of fishes ; 2. the so-called pseudonavicella of worms, etc. (both are pronounced to be the granular germs of gregarinæ ; to us they are of no interest) ; 3. the so-called oval or globular psorospermiæ ; 4. the so-called Miescherian pouches.

The globular psorospermiæ were first found by J. MÜLLER (Arch., 1841, p. 477, etc.), then by HAKE (A treat. on varic., capill., etc., 1839) and NASSE (Müll. Arch., 1843, p. 209) in the liver of rabbits, by REMAK (Diagnost., etc., Unters., 1845), in the intestines of rabbits. LIEBERKÜHN (Mém. de. l'Acad. Royale. de. Belg., 1854), and STIEDA (Virch. Arch., 1865, XXXII., p. 132) first conjectured their relation to gregarinæ. Consult also KLEBS (Ib., 1859, XVI., p. 188). WALDENBURG (Ib., XL., p. 435) still more positively fixed their character as that of psorospermiæ. See also VIRCHOW (Arch. XLIII., p. 548, etc.). Wholly different views are held by ROLOFF, H. JONES, LANG (Ib., XLIV., p. 202). According to ROLOFF (Med. Centralbl, 1868, No. 21, and Virch. Arch., XLIII , p. 512) these and the larger analogous forms within and near the muscles of the mouth in sheep are not psorosperm pouches, but accumulations of lymph-corpuscles. These lymph-corpuscles wander out from the perimysium internum into the muscular fibres and, when they have aggregated into masses, they become surrounded by an enveloping membrane.

According to EIMER (Ueb. d. Psorospermien u.s.w., 1870) psorospermiæ are not granular germs of gregarinæ, but gregarinæ at rest, from which by folding the proper psorospermia arise. The sickle-shaped animalcule, the gregarina, becomes within or without the mother-vesicle, an amœboid cell. The latter grows, free or within an epithelial cell, and finally become a so-called naked psorosperm. i. e., a round or oval granular body with or without nucleus. It becomes encapsuled ; within the transparent capsule, there appears yet a second sheath. The capsular content contracts into a small globule, which divides into small furrowed globules. From these arise the young gregarinæ. The capsules burst, and the gregarinæ become free. Gregarinæ or amœbæ arising therefrom frequently enter the epithelial cells of the intestines, there to develop, and thence to pass into other parts of the body, especially the liver. See also RIVOLTA (Il. medico veterin., March, 1869).

In man psorospermiæ have been found in the intestines by KJELLBERG (Virchow Arch., XVIII., p. 527) and EIMER, in the liver by GUBLER (Gaz. méd., 1858, p. 657), DRESSLER (LEUCKART. Die menschl. Paras. 1., p. 740), in the kidneys and in the urine by LINDEMANN (LEUCKART. Ib., p. 741.)

The so-called MIESCHER'S pouches or RAINEY'S corpuscles in the muscles of hogs, etc., consist of a dark granular mass, 1 mm. and more in size, of oval form, which, surrounded by a transparent capsule, appears imbedded within a primitive muscle-bundle, and gives rise to a slight oval protrusion. They sometimes look like trichina capsules, but never contain a worm.

FLAGELLATÆ. Organisms without a mouth, similar to the infusoria, whose motor organs are formed of many lash-like cilia, rarely, at the same time, by a temporary series of cilia.

FAM. MONADINA. With round or oval transparent bodies, devoid of distinct organization, with a single or only a few glittering, whip-like hairs on the anterior extremity.

CERCOMONAS, (DUJARDIN.) With a caudal filament, and, for the most part, with a single long and thin lash.

CERCOMONAS INTESTINALIS, (LAMBL.) Found by DUJARDIN and others in the stools of typhoid fever and cholera, by LAMBL on the catarrhal mucous membrane of children.

CERCOMONAS URINARIUS, (HASSAL.) In the urine in cholera, in alkaline, albuminous urine.

' Cercomonas saltans, (Ehrenberg.) Observed by Wedl on the dirty surface of ulcers.

Trichomonas, (Donné.) Differs from Cercomonas in having some short cilia, one, two, or three near the anterior lash.

Trichomonas vaginalis, (Donné.) Very common in blenorrhœa of the vagina, especially in the yellowish, strongly acid vaginal mucus.

II. Vermes. worms.

Laterally symmetrical animals, with non-articulated bodies, composed of curved, or homogeneous segments without articulate appendages (limbs). The embryo is generally formed by a transformation of the whole yolk, without previous primitive folds.

The skin consists of a layer of cells and mostly of a superficial homogeneous chitin layer, which constitutes one of the secretitious variously strong cuticula. The derma, through the attachment of the longitudinal, and often also of the transverse muscles, becomes a cutaneous muscular pouch, the most important organ of motion. Often there is an entire absence of appendages. When they exist, they consist either of apparatus of prehension (suckers and siliceous hooks), or bristly tufts. Sometimes gills are found, without which respiration is carried on by means of the skin. Their abode is in water or in moist localities; their motion is generally slow. Besides worms without intestinal canal, blood, and nervous systems, there are found others which possess these apparatus in highest perfection. The organ of excretion is the so-called water-vessel system, i. e., a symmetrically divided canal of finer or coarser caliber, filled with a watery, sometimes granular liquid, and terminating externally by a single or multiple orifice. For the most part the very important organs of generation, male and female, are separate in different individuals; sometimes they are united in the same body. Their development is, as a rule, connected with a metamorphosis. To worms belong the most numerous and most dangerous of human parasites. They live exclusively in the internal organs.

1. Class: Platodes, Platyelmia, Flat Worms.

Worms with bodies more or less flattened, whose appendages, when present, consist mostly of suckers and hooks. They are mostly hermaphrodite. Nearly always, at least temporarily, parasitic. Many are without mouth, intestines, and anus, so that the nourishment is taken up through the surface of the body.

First Order : Cestodes, Tape-worms.

Long, articulated, flat worms without mouth and intestinal canal, with organs for prehension on the anterior extremity.

The anterior part lessens in size and presents a button-like or globular swelling, the so-called tape-worm head, which, in different ways, bears various organs of prehension. The thinner portion of the body immediately behind the head, the so-called neck, shows generally at some distance from the head the first marks of an articulation. The first yet indistinct rings, farther on shorten and constitute the joints, then, in continuous succession these lengthen and broaden, and at a greater distance from the head become sharply defined and distinct from one another. At the posterior extremity the articulations reach their greatest circumference, often separate from the body of the worm, and live a long time independently as isolated so-called proglottides. The tape-worm is also looked upon as a

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chain of animals, consisting of the articulations, the proglottides, the individual, and the sexual animal. These develop by means of alternate generation by a process of budding, on the pear-shaped parent, the head (SCOLEX), and hang thereon together to form a long and ribband-like colony (commonly called *tape-worm*). The parenchyma of the body, enclosed by a tender skin and subcutaneous muscles, is a cellular connective tissue, which, in its periphery, especially on the head, incloses small chalky concretions, in all parts, the ramifications of water-vessel system, and in the central parts, the sexual organs. Organs of sense are wanting. Likewise is there no digestive canal: the nutritive liquid ready for absorbtion enters by endosmosis directly into the parenchyma of the body through the whole outer surface. The water-vessel system, passing through the whole length of the body, serves as the apparatus for excretion. There are at most two or four longitudinal canals, laterally situated, which, in the head, communicate with one another by transverse loops; also in the single articulations transverse anastomoses exist, and they empty their contents through a pore in the end segment. Every segment of a tape-worm has its special male and female organs of generation. The male portion consists of numerous pear-shaped testicular papillæ whose pedicles lead into a common secretory duct. The winding end of this lies in a muscular sac (*cirrusbeutel*), and may project out of it as a curl through the opening of the generative organs. The female genitals consist of an ovary, uterus, seminal vesicle and vagina, which last, for the most part, beneath the opening of the male organs, usually empties exteriorly in a common drain. With the great increase of the articulations and their distance from the head, the perfection of the sexual apparatus increases gradually from the anterior to the posterior extremity of the worm. The posterior segments ripe for separation are the first to perfect their whole sexual development. All tape-worms are oviparous; but the embryo is often developed in the egg within the uterus.

Human tape-worms exhibit a complicated metamorphosis connected with alternate generation. Generally the ova with the proglottides leave the intestines of the tape-worm bearer (man), and are present on manure, plants, in water, etc., and are thence passively conveyed with the food into the stomach of an animal, rarely of man. After the sac of the ova has been destroyed in the new abode by the operation of the juices of the stomach, the embryos become free in the stomach, and by means of their four or six movable hooklets bore through into the vessels of the stomach and intestine. Here they are driven along by the blood-current and deposited in the capillaries of the most various organs (liver, muscles, brain, etc.). After the loss of the hooklets, the embryos, mostly encapsulated in a cyst of connective tissue, grow into larger vesicles, which consist of an external contractile parenchyma and watery contents. The vesicle gradually becomes the cyst-worm. From its covering one (*cysticercus*), or several (*echinococcus*) nodular depressions grow into the interior, on the bottom of which is supported the armament of the tape-worm's head, in form of suckers and wreaths of hooks. These depressed nodules turn outward, so that they appear as external appendages of the cyst, presenting the form and size of the tape-worm's head with more or less developed neck. It is necessary for the cyst-worm to enter the intestinal canal of a new animal (*e. g.* of man), to allow the head, after its separation from the wall of the cyst-body, to assume the condition of a sexually-mature tape-worm. This transportation is passive throughout, effected by means of the food, especially by the use of measled meat. The cyst is digested in the stomach, and the head

of the tape-worm is set free as a scolex ; the latter enters the small intestines, fastens itself by means of its prehensile apparatus to the intestinal wall, and develops by gradual formation of segments into the body of a tape-worm.

All tape-worms inhabit the small intestines, while the cyst-worms may dwell in the most various organs.

FAM. : TÆNIADÆ.

The pear-shaped or conoidal head bears four round suckers with powerful muscular apparatus. Between the suckers is commonly placed on the advanced median portion of the head the *rostellum*, a single or manifold wreath of claw-shaped hooks, for whose special motion a muscular apparatus is provided. Two sexual openings, one male and one female, which latter serves only for coition. The ova can become free only through the proglottides, since the uterus has no special opening. The proglottides are distinctly separate from one another, in the perfected state for the most part longer than broad, and are commonly provided with sexual openings upon the border.

A. VESICULAR TAPE-WORMS :—CYSTICÆ.

Most are of considerable size. The head only rarely unarmed (tænia mediocanellata) otherwise provided with a lenticular, slightly prominent *rostellum* and a circle of hooks. Besides the claws, the hooks have two strong projections from the roots, the shorter one anterior, the longer posterior. The proglottides are in the perfect state, elongated oval. The middle stem of the uterus gives off a number of ramifying side-branches. The openings of the sexual apparatus are on the border, regularly alternate, sometimes to the right, sometimes to the left. The ova have a firm and brown shell. The embryonal hooks are short and thin.

a. VESICULAR TAPE-WORMS, whose heads are formed in the embryonal state (Subgen. *Cystotæniæ*,—LEUCKART).

TÆNIA SOLIUM, (LINN.)

Inhabits the small intestines. Occurs more often, singly ; less frequently, several are together ; very rarely, numbering from ten to forty and over. In the developed state is usually from two to three metres long, and its proglottides 10 mm. long, and 6 mm. broad. The head is of the size of the head of a pin and globular, with tolerably prominent suckers. The vertex is not infrequently pigmented black, and bears a moderately large rostellum with about twenty-six hooks. Beyond the head follows a neck, almost an inch long, filamentous and finely articulate. In the beginning the articulations are short, but their length gradually increases, so slowly however, that they first assume the quadratic form at a distance of one metre behind the head. Not far beyond begin the mature articulations. The mature proglottides which come off only with the excrement, at first in about three to three and a half months after infection (in different persons, in irregular numbers and times), are longer than broad, with rounded corners, like pumpkin seeds. The openings for the sexual organs lie behind the middle. The uterus possesses from seven to ten side branches which divide into a varying number of dentated branches. The ova are nearly round and have a thick shell.

The CYST-WORM (*cysticercus cellulosæ*) belonging to this species has an especial preference for the muscles of the hog, but is found also in other

places and in other animals, seldom in the ape, dog, deer, rat, etc.   In man it is found most frequently in the intermuscular and subcutaneous connective tissue, and in the brain, more rarely in the eye, heart, lungs, liver, kidneys, meninges of the brain, and lymphatic glands, very rarely in the spleen and bones.   Its occurrence in animals is usually in masses.   In man it is found sometimes single ; sometimes several are found, rarely in vast numbers. The tail-cyst has an irregular, moderate size, and in the muscles, a transversely elliptical form with the longest diameter in the direction of the course of the fibres ; in soft organs (eye-chambers, vitreous, ventricles of the brain) it is round.   The full development of the parasite continues two and a half months ; its life, from three to six years.

The derivation of *tænia solium* from the common measle-parasite of swine follows not only from the entire agreement in the formation of the head and form of the hooks, but is also experimentally proven, by the development of the *cysticercus cellulosæ* out of the ova of *t. sol.* ; also, by the growth of the tape-worm in the intestinal canal of man, from the *cystic. cell.* (KUCHENMEISTER).

Once I found cysticerci in large numbers, in the earlier stages of development, in the liver of a tuberculous man 36 years old.

TÆNIA MEDIOCANELLATA, (KÜCHENMEISTER.)

Surpasses the tænia solium, not only in length (by one meter), but also in breadth and thickness, as well as in the size of the proglottides.   Particularly striking is the breadth of the immature segments, which sometimes reaches from 12 to 14 mm., and, behind the head, they rarely diminish so preceptibly as in t. sol.   The length of the segments increases much more slowly than in the latter.   The head, of considerable size, is without a circle of hooks and rostellum, with a flat vertex, and four large, extremely powerful suckers, which are usually surrounded by a border of black pigment.   The complete development of the sexual organs is found as in t. sol., near the 450th segment, while the proglottides reach maturity in only from 360 to 400 segments farther.   The ova have a thick shell and are mostly oval.   The uterus is characterized by the number (20–35) of its lateral branches, which lie close by the side of one another, and instead of by dendritic branching, they are known by their dichotomous division. If, as here very often happens, the segments come away spontaneously, they are usually without ova and shrunken, but still always of considerable size and thickness.

The CYST-WORM of this species inhabits the muscles, especially also the heart and internal organs of cattle ; it is similar to the measles of swine, but smaller and without circles of hooks.   It does not yet appear to have been found in man.

TÆNIA (CYSTICERCUS) ACANTHOTRIAS, (WEINLAND.)

The vesicles of this tape-worm, which have hitherto alone been known, live like the *cysticercus cellulosæ*, which it closely resembles, in the muscles, subcutaneous connective tissue, and brain of man.   The hook-apparatus consists of a triple circle of quite slender claws.

TÆNIA MARGINATA, (BATSCH) : from *cyst. tenuicolli*.

The mature tæniæ, which are found in the dog and wolf, bear a resemblance to tænia solium.   The larva (*cyst. tenuicollis*) abides especially in the omentum, less frequently in the liver of the ruminants and swine, and occasionally in that of man (*cystic. visceralis* of authors).   It is oval, and of considerable size.   In the fully grown larva, one extremity of the vesicle is drawn out into a neck-like process of greater or less length, which process contains a solid tape-worm, and surrounds it

like a sheath, when both are drawn into the interior of the vesicle. The posterior extremity grows riband-like, and hangs loose in the vesicle.

b. CYST-TAPE-WORMS, whose heads bud forth from the embryonic capsules attached to the inner surface of the vesicle.

TÆNIA ECHINOCOCCUS, (V. SIEBOLD.)

The worm, three to four mm. long, consists of only three or four segments, the last of which, at maturity, exceeds in bulk the whole remaining body. The thirty or forty hooklets have coarse processes at their base, and are placed on a tolerably prominent rostellum. It lives in numbers in the intestinal canal of the dog (not in man).

The young state of this tænia, the so-called ECHINOCOCCUS, forms a very considerable, almost motionless vesicle, which consists of a laminated cuticle, and of the underlying cellular parenchymatous layer, upon the inner surface of which numerous little heads bud forth in vesicles of the size of a millet seed. Not infrequently the vesicles increase by a budding process, outward or inward, thus being transformed into a compound system of larger and smaller vesicles inclosed one within the other (daughter, granddaughter- etc., vesicles), all of which in turn give rise to a head. In this form the vesicles are found in man and cattle (so-called *echinoc. hominis, s. altricipariens, s. endogenus, s. hydatidosus* of the authors), while the remaining ruminants, swine and apes, for the most part harbor single vesicles, or those which increase exogenously (so-called *echinoc. veterinorum, s. exogenus, s. granulosus, s. scolicipariens* of the authors). The favorite abode of the echinococcus is the liver in man, yet it is occasionally found in almost every organ (subcutaneous cellular tissue, muscles, peritoneum, kidneys, lungs, spleen, nerve-centres, bones, heart, orbit and eye, thyroid, etc.). The *echinoc. granulosus* is found most often in the epiploon, in the parietal layer of the peritoneum and in the bones, less often in the liver, spleen, lungs, etc.; the *echinoc. hydatidosus*, preferably in the liver, spleen, lungs, and subcutaneous cellular tissue; sometimes two forms occur in the same body and even closely united—generally a single echinococcus only is found; many occur in various organs, the liver, however, being usually the principal habitat.

According to LEUCKART, the distinction between *echinococcus altricipariens* and *e. scolicipariens* is inadmissible, since both come from *tænia echinococcus* (KRABBE'S Erfahrungen aus Island; NAUNYN's Experiments, *Arch. f. Anat. Phys. u. wiss. Med.* 1862).

The echinococcus of the liver occupies any part of the organ. In half of the cases of echinococcus of the liver which I have seen, it had become effete in various stages. Twice in the greater omentum I found movable echinococci, and on all the surfaces between the layers, shifting effete echinoc., of the size of a cherry. Consult also VIERTEL, *Ueb. d. Vork. v. Echinoc. im Knochen-system des Menschen.* Breslau, 1872.

The growth of the echinococcus is mostly a slow one, continuing, not infrequently, for ten years, as has been determined by experiment, from the diagnosis of accessible echinococci of internal organs, as well as especially from their presence in the subcutaneous cellular tissue. An *echinococcus hydatidosus*, nearly as large as a child's head at the time of operation, situated subcutaneously between the crest of the ilium and ribs of a man forty-one years old, had been observed in his twelfth year having the size of a musket-ball. The growth was somewhat quicker in another similar case.

While the above-mentioned forms of echinococcus always represent a vesicular body of considerable size, the so-called multilocular echinococcus (VIRCHOW) is always small, of the size of a millet-seed, or, at the most, of a pea. Observed from

the earliest period of its development, it is never found to form a single vesicle, but only a group of little vesicles, which, larger and smaller intermixed, lie close to one another in considerable numbers, the smallest portion forming heads, and are embedded in a common stroma. It has hitherto been observed only in the liver, where it for the most part forms a round, firm body from the size of the fist to that of a child's head, which is quite easily deprived of its covering, resembles many colloid tumors combined, and, on this account, was formerly regarded as alveolar This echinococcus shows in section, many small, mostly irregular cavities, separated from one another by a more or less thick quantity of connective tissue, which cavities enclose a tolerably transparent gelatiniform contents. The substance of the liver has there entirely disappeared. The multilocular echinococcus in particular has a great disposition to central ulceration.

HUBER (*Virch. Arch.*, 1872, LIV. p. 269) saw a multilocular echinococcus of the right supra-renal capsule.

B. COMMON TAPE-WORMS:—Cystoideæ.

These represent, in their early state, no peculiar larvæ. In the larval state (cysticercoidæ) they occur only in the cold-blooded animals, especially invertebrates. (Thus *e. g.* the cysticercoid of *tænia elliptica, s. cucumerina* of the dog live in the lice which infest dogs: the dog infects himself by eating these lice.) With respect to the tape-worms themselves, the small size of the head and the imperfect development of the hook-apparatus are especially deserving of notice. Clinically, they are of less importance than the cyst-tape-worms.

A. The prominence on the head is supplied with a single circle of small hooks. The genital pores are unilateral; there is a small number of vesicular testicles and a large receptaculum on the short vagina. Vas deferens without coils. Uterus large, extending through the whole joint. The ova show two smooth shells, and contain an embryo with large hooks.

TÆNIA NANA, (V. SIEBOLD.)

Small, about 2.5 cent. long, 0.5 mm. broad. The body anteriorly, filamentous, but becomes quickly larger near the middle. Consists of a head and about one hundred segments, the last of which contain twenty to thirty mature ova. Once found by BILHARZ in the duodenum of a boy.

TÆNIA FLAVO-PUNCTATA, (WEINLAND.)

Is 33 cent. long. The anterior half consists of immature joints, 0.2 to 0.5 mm. long and 1 mm. broad, which show behind the middle a quite large yellow spot, the receptaculum filled with sperm. In the remaining half the joints grow to the length of 1 mm. and breadth of 2 mm., are without yellow spots, but through the moderate development of the ova they are brownish-gray. The mature joints are trapezoidal, sometimes almost triangular. Head, unknown. Found once by WEINLAND in a child nineteen months old.

B. The club-shaped papilla is provided with a multiple circle of small hooks, with a disk-shaped base. Two genital pores, opposite to each other. open into a male and a female duct, the latter of which, besides a receptaculum, possesses several germ-forming organs.

TÆNIA ELLIPTICA, (BATSCH.)

Usually in dogs and cats. In the mature state, 150 to 200 mm. long and, behind, 1.5 to 2 mm. broad. The anterior extremity of the body is thin, filamentous, with a thick head. The first forty joints are short; thereafter they stretch out so that the last are three or four times longer than broad, and are so nearly isolated from one another that the worm behind resembles a chain. The most mature joints have a reddish color from the ova.

FAM. : BOTHRIOCEPHALIDÆ.

Head flattened; its surface perpendicular to the surfaces of the series; provided on its borders with two deep fissure-like suckers. Articulation of the

body only imperfectly marked. Proglottides mostly broader than long. Three genital openings : one male and two female (*i. e.*, one opening of the vagina and one of the uterus), on the middle line of the abdominal surface of the articulation. The hard shell, already provided before the commencement of the formation of the embryo, is provided with a lid so that the four or six-hooked embryo may come out independently, and float about free for a long time with the help of a ciliary covering.

BOTHRIOCEPHALUS, (BREMSER.)

With a long-jointed body and hookless head. The genital pores are on the surface of the joints, over the uterus, near their anterior extremity. The mature uterus has the form of a rosette.

BOTHRIOCEPHALUS LATUS, (BREMSER.)

The most considerable human tape-worm, which sometimes is from 5 to 8 metres in length, and then consists of from three thousand to four thousand short and broad joints. The length of the joints, with the exception of the last, is seldom more than 3.5 mm., while the breadth at the middle gradually increases to 10 or 12 mm. In the latter half the breadth diminishes, while the length increases, so that the last joints are nearly square. Here the body is thin and flat, like a riband, especially on the sides, while the central part of the single joints stand out in the form of an elongated roll. The anterior end grows smaller and smaller until it at last becomes thread-like (0.6 mm.), so that the head, 2.5 mm. long and 1 mm. broad, terminates in form of an oval swelling. The first mature ova are found at a distance of 500 mm. behind the head. The proglottides are not passed away singly, but in lengths (from 2 to 4 feet), especially in February, March, October, and November. However, at every stool the characteristic ova of the tape-worm pass away : these are oval ; their shells, transparent, colorless and single. The ova have a lid at one pole of each ovum, through which, when it is opened, the embryo slips out into the water. At the time of coming away, they are always in that stage of development represented by folds of the yolk. The six-hooked embryo, which is embedded in an outer ciliated membrane, is first developed several months after the ova have been passed from the intestines, and, indeed, in fresh water (*i. e.*, river or sea-water). It differs from that of the Tæniæ by its globular form, and by a firm membrane provided with thick cilia.

The *bothr. latus* is found only in the western cantons of Switzerland and the adjacent districts of France, in the north-western and northern provinces of Russia, in Sweden and Poland, less frequently in Holland and Belgium, in single districts of eastern Prussia and Pomerania, Rhenish Hesse, indigenous also in Hamburg, Berlin, London, etc. All these countries and localities are characterized by bodies of water ; they are either bounded by coasts, or low countries with larger seas and rivers.

According to KNOCH (*Virch. Arch.*, XXIV. p. 453) the embryos of the *bothr. latus* are developed from ova in fresh water, in which also they travel. In river water, which especially in the western provinces and cities of Russia is used for drink, they are conveyed into the intestinal canal of mammals, and are then, after some time, developed into sexually mature tape-worms. The feeding of various fishes with the ova of the *bothr. lat.* have determined nothing with certainty respecting its scolex. While the embryos of *tæniæ* become the sexually mature tape-worm only after passing through the stage of vesicle, the embryo of the *bothr.* is transformed in the intestine into the sexually mature animal without the preceding vesicular state. There is

therefore no doubt that the broad tape-worm is conveyed to man by drinking-water, and for the most part in the form of an embryo.

BOTHRIOCEPHALUS CORDATUS, (LEUCKART.)

Not unlike the *b. latus* in the formation of its joints, but much smaller. The head, short and broad, heart-shaped, with level mouths. The broad body, with its segments, follows immediately, which increases so quickly that the anterior part of the body assumes the shape of a lancet. The mature segments are from three to four mm. long; the last larger and almost square. It is found in northern Greenland.

Second Order : Trematodes, Sucker-worms.

Parasitic solitary flat-worms, with inarticulate leaf-shaped bodies ; with mouth, and bifurcated intestinal canal without anus; with abdominal prehensile apparatus.

With respect to the basis substance, the skin and muscular apparatus have the same relations as in the tape-worm. On the anterior pole of the body is the mouth, for the most part at the bottom of a sucker. This leads into a muscular pharynx and œsophagus, which is continued into the always blind intestine. The excretory apparatus consists of a network of fine vessels, and two larger lateral branches discharging on the posterior pole. They contain a liquid with granular concretions. The organs of prehension vary with the manner of life, etc. Male and female organs are mostly united in the body of the same individual. Their pores open near the middle line of the forepart of the surface of the abdomen. In the ovaries the ova accumulate in great numbers and complete the stages of embryo-formation. All trematodes discharge their ova. The young having escaped, in the distomata go through a complicated alternate generation connected with metamorphosis. The small contractile, naked or ciliated embryos slip out of the ova which have reached water, and, wandering independently, seek a new animal habitat, mostly snails. They pierce into their interior, lose their cilia, and then develop into germ-cysts. These are the parents of the CERCARIÆ, which are provided with a rudder-like tail, and having escaped from the parent cyst and its habitat, move about free by creeping or swimming in water. They then enter a new aquatic animal (snails, worms, crabs, fish), into the tissues of which they pierce their way, and after the loss of the tail, form about themselves a cyst. Thus have the encysted, young, sexless distomata arisen from the cercariæ; the former received with the flesh of their supporters into the stomach, and thence, freed from their cyst, they enter other organs of another animal, where they become sexually mature. Usually the various development-stages of the distomata have also three different habitats.

DISTOMUM, (RUDOLPHI.)

With two suckers on the anterior part of the body. Near the abdominal suckers lie the genital pores. The internal organs of generation occupy the hind part of the body.

A. Body broad and leaf-shaped, with the forepart prominent and beak-shaped. The uterine coils twist into a rounded body behind the abdominal sucker. Testicles and intestine branched ; the former strongly developed.

DISTOMUM HEPATICUM. LIVER-FLUKE.

Upon the tolerably thick forepart of the body (4 to 5 mm.) follows a flattened, elongated oval, larger part, which quickly grows to a considerable breadth (12 mm.), then becomes smaller, and not infrequently reaches a length of from 25 to 28 mm. The cuticula bears a great number of scaly spines. Suckers small and weak. Between the two is the genital pore, out of which comes the thick, horny, spiral penis. The uterine coils appear as a dark brown spot through the dirty-yellow surface of the

body, close behind the abdominal sucker. Also the branches of the intestinal canal often show a blackish color. The lateral borders of the body posteriorly contain the granular ovaries.

The cercariæ of *distomum hepaticum* and *lanceolatum* are encapsuled most probably in fresh-water snails (*planorbis*), which if, *e. g.* in marshy places, they are eaten by sheep, the latter become infested by them.

The perfect *dist. hepaticum* inhabits numerous herbivorous mammals, especially sheep and other ruminants; also the horse, ass, swine, rabbit, squirrel, etc., and, but seldom, man. Its usual abode is in the biliary ducts, especially the largest; much less often in the intestines, in the interior of the vena cava, and other parts of the venous system. It occurs in man, for the most part, singly or in small number, and in all the detailed cases were the cause of obstructing the flow of bile; while in most domestic mammals they have sometimes been found in such numbers that dilatation of the biliary ducts, atrophy of the liver, emaciation, dropsy, and death have resulted (so-called liver-rot). Also in abscesses of various parts of the body, the liver-fluke has been found in a few cases.

B. Body more regularly formed, without branched intestinal canal. The uterine coils reach to within longer or shorter distance from the posterior extremity of the body, often to it. The hind part of the body is moderately broad and flattened.

DISTOMUM CRASSUM, (BUSK.) Once found in the intestinal canal.

DISTOMUM LANCEOLATUM, (MEHLIS.)

With thin bodies from 8 to 9 mm. long. Both extremities of the body pointed, the anterior more so, so that the posterior half has a greater breadth (2–2.4 mm.). The part between the two suckers passes gradually into the other portions of the body. The oral, like the abdominal sucker, has a central position. The shield-like prominent border of the head is pierced by numerous gland-pores. The head is naked. Both lobed testicles lie closely behind the abdominal sucker, before the ovary and the strongly developed uterus, whose coils shine through clearly. The anterior coils which contain the mature ova are black, the remainder rusty-red. The penis is long and filamentous. The embryo, which is almost completely developed in the interior of the uterus, is oval or spherical, ciliated anteriorly, and provided with a spikelet on the vertex of the head.

Its abode, like that of *dist. hepaticum*, with which it is often associated, is in the bile-ducts, especially the small ones, sometimes also in the gall-bladder and intestines of sheep and cattle; seldom in deer, rabbits, hares, swine, and extremely seldom in man.

DISTOMUM OPHTHALMOBIUM, (DIESING.) Once found in the crystalline lens.

DISTOMUM HETEROPHYES, (SIEBOLD.) Twice found by BILHARZ, in Egypt, in very large numbers in the small intestines.

C. With separate sexual apparatuses. Bodies long and slender; in the female almost cylindrical; in the male, the back part of the body flattened and involuted.

DISTOMUM HÆMATOBIUM, (BILHARZ.)

Oral and abdominal suckers of equal size, near to one another, on the anterior part of the body. The genital pore close behind the abdominal sucker. Color, milk-white. The male is shorter (12–14 mm.) and thicker than the female, and has larger suckers. The anterior part of the body which bears the suckers is distinctly flattened, while the posterior, which quite suddenly thickens, appears cylindrical, but upon closer examination is found to be flattened. The apparent cylindrical form arises from a furrow-like incurvation of the abdominal surface. The folded body posteriorly forms an incompletely closed tube for the reception of the female. The male genital organs consist of thickly crowded seminal vesicles, provided with a single duct. The surface of the body is covered with little spikelets. The female has a long (14–19 mm.) and slender, almost cylindrical body. The intestinal canal divides for only a short distance, and then its diversions together enter a single blind pouch, near to which the ovaries extend. The elongated oval ovary forms at the posterior extremity a canal, which, joined with the oviduct, extends to the genital pore. The embryo is cylindrical, and terminates anteriorly in a pointed proboscis; its surface is covered with thick cilia. Any farther metamorphosis is unknown.

The *dist. hæm.* is very frequent in Egypt: In the vena portæ and its branches, the splenic veins, the mesenteric veins, as well as in the textures of the intestinal canal and bladder. Its food is the blood, the corpuscles of which are always found in its intestine. In the vessels it causes various anatomical obstructions; in the mucous

membrane of the bladder, ureters, and of the intestinal canal, hyperæmia, hæmor-
rhage, pigmentation, nodules, pustules, and ulcers resembling those of dysentery or
condylomatous excrescences ; sometimes obstruction of the ureters with consecutive
formation of calculi, pyelitis, and hydronephrosis.   According to GRIESINGER (*Arch.
d. Heilk.* 1866, p. 46), exotic hæmaturia, at least at the Cape of Good Hope, is due to
dist. hæm.

MONOSTOMUM, (ZEDER.)

Differs from *Distomum* chiefly in the absence of the abdominal sucker.   The oral
sucker also has only a slight independence ; the pharynx, usually very well developed.
The genital pores are near the anterior extremity.

MONOSTOMUM LENTIS, (NORDMANN.)   Once found in the crystalline lens.

2.   CLASS : NEMATELMIA, ROUND-WORMS.

Worms with rounded, pouched, or filamentous bodies, without rings or
segments, sometimes with papillæ or hooks on the anterior pole. The sexes
are distinct.

FIRST ORDER : ACANTHOCEPHALI.

Pouched round worms with rimmed vertex bearing hooks, without mouth
and intestinal canal.

The chief species, ECHINORRHYNCHUS, inhabits the intestinal canal of several of
the vertebrates.   One of this form, not yet sexually mature, was found by LAMBL in
the small intestines of a leucæmic child.

SECOND ORDER : NEMATODES, THREAD-WORMS.

Round worms with lengthened, thread-like bodies, with mouth and
intestinal canal.

The armament, when present, consists of papillæ in the neighborhood of
the mouth, or of spikelets and hooks within the oral cavity.   The mouth,
on the anterior extremity of the body, opens into a narrow œsophagus,
which, for the most part, dilates into a muscular pharynx.   Then follows
an intestinal tube with cellular walls, which terminates on the abdominal
surface, not far from the posterior extremity of the body, in the anus.
The hard skin, often transversely wrinkled and consisting of many layers,
incloses the strongly-developed muscular layer.   There are two lateral
longitudinal striæ of free muscles, the so-called side-lines, *i. e.*, organs of
excretion analogous to the water-vessel-system, which together open, by
means of the transverse vessel-pore, so-called, at the upper part of the
pharynx on the abdominal surface.   A nervous system in form of a ring
around the œsophagus, is in many certainly demonstrated.   They are
sexually distinct.   The male differs from the female in its smaller size, and
generally by the curled posterior extremity of its body.   The male and
female genitals are extended, forming single or coupled pouches, which, in
the upper portions, represent testicles and ovaries, in the lower portions
ducts and reservoirs for the procreation material.   These coupled ovarian
pouches are placed upon a short vagina common to both, which opens
through the female genital pore in the middle of the body, or near the
anterior or posterior pole.   The male genital pore is situated at the poste-
rior end of the body, and possesses an organ for copulation protected by
prominent spiculæ.   The nematodes are partly oviparous, partly viviparous.
The free development of the young forms takes place mostly by single meta-
morphosis ; it is nevertheless often complicated, so that it does not always
occur in the habitat of the mother animal.   Many young forms have an

abode altogether different from that of their parents, and often the young and sexually mature nematodes inhabit different organs of the same animal, or even different animals. The transportation of the free and parasitic development-forms distributed to different organs of different animals, is partly by means of their own wandering, partly in a passive manner by means of the food and drink. Some nematodes live parasitically in parts of plants.

1. SUB-ORDER : STRONGYLOIDÆ, NEMATODES WITH ANUS.
1. FAM. : ASCARIDES.

Mouth provided with three lips or papillæ, sometimes with horny borders and teeth in the throat. Opening for the penis near the posterior end with a point going out from the pointed tail. Most of the forms of ascaris lay hard-shelled eggs, which develop into an embryo only after a long abode in moist media.

ASCARIS LUMBRICOIDES, ROUND-WORM.

Body cylindrical, pointed at both ends, whitish or reddish in color. The length of the male reaches 250 mm.; thickness, 3 mm.; the length of the female, 400 mm.; thickness, 5.5 mm. The skin is transversely marked, with four whitish longitudinal striæ. The head, consisting of three semi-lunar lip-shaped parts, is separated from the body by a groove. The tail of the male is conical and hooked, that of the female, blunt. The male genitals are situated anterior to the tail; those of the female, anterior to the middle of the body. The intestinal canal runs through the whole body and opens near the tail. The remaining cavities of the body are occupied, in the female, by the white filamentous genitals (with about 60 mm. ova), which, in injury to the animal, are pressed out ; in the male, by the testicle and seminal duct. It occurs very often, especially in children from three to ten years of age, and especially in autumn. Its chief habitat is the small intestines, whence it may wander into every part of the intestinal canal from the mouth to the anus, seldom into the gall, and pancreatic ducts, and upper respiratory tubes. In the small intestine and other parts, the round worm may occur singly or in small numbers ; but in the small intestine they may exist in very large numbers (one to two hundred and more). They wander spontaneously in health or during some diseases (typhoid fever, cholera, etc.), to the exterior of the body. The harm which these worms may cause, consists in catarrh of the organs of digestion, some-times in nervous phenomena (paleness of the face, dilatation of the pupils, etc., and convulsions of various kinds), and in stenosis of the narrow passages, causing icterus, suffocation, etc. They seldom cause perforations of the intestinal walls and the so-called worm-abscesses of the abdominal wall, especially in the umbilical and inguinal regions, which contain pus, one or more round worms and usually food or excrement, and are evacuated for the most part exteriorly, seldom with the urine. Still more rarely do they give rise to acute general peritonitis.

ASCARIS MYSTAX, (ZEDER.) ASC. ALATA, (BELLINGHAM.)

Smaller and thinner than the preceding, quite regularly symmetrical. The female, to 120 mm. in length; the male, to 60 mm. Identical with the common round worm of cats. Observed only a few times. Sequelæ little known.

OXYURIS VERMICULARIS, THREAD-WORM.

Body filamentous, white. On the head are three lips and strong cuti-

cular swelling. The females exist in much larger number than the males. The length of the male is 4 mm.; that of the female, 10 mm. Skin striated, with tooth-like prominences. The tail of the male blunt and curled, with a sucker on the point; that of the female, occupying a fifth of the length of the body, pointed and straight. The straight intestinal canal runs through the middle of the body. The male genital pore is near the tail; that of the female, in the anterior half of the body. They occur very often in children, not infrequently in adults, in greater or less number, and continue sometimes only a short time, sometimes years. They inhabit preferably, the rectum or the whole large intestine, seldom the lower part of the small intestine. Sometimes they are found around the anus and in the vagina.

Worms excite catarrh in the intestine and itching around the anus, especially at evening, when they partly leave the rectum and go even into the vagina. In consequence of the itching arise nervous excitements, excoriations, eczema, etc., and, in the vagina, catarrh.

2. FAM.: STRONGYLOIDÆ.

Mouth for the most part armed with a horny surface or hooks. Penis embraced by a bell-shaped vesicle.

STRONGYLUS (EUSTRONGYLUS) GIGAS.

Very long, cylindrical, red worm. Viviparous. The male hardly .5 M. long, 12 mm. thick; the female from 100 mm. to more than 1 M. long, 8–12 mm. thick. The body blunt posteriorly; anteriorly, pointed. The mouth narrow, surrounded with six papillæ. The female genital pore far forward. It is distinguished from all the other male nematodes by its length, but chiefly by its blood-red color, but is easily mistaken for the fibrin of blood-clots. Smaller specimens can also be confused with asc. lumbricoides. It is rare. It occurs in the pelvis of the human kidney, which it obstructs, as well as in the parts surrounding the kidney. Out of the former locality the worm can be expelled with the urine; out of the latter, it may reach the exterior by causing the formation of abscesses. In the kidneys, abdominal cavity and heart of the dog, and of beasts of prey.

STRONGYLUS LONGEVAGINATUS, (DIESING.)

Body filamentous, straight, dirty white, longitudinally striated. The male 12–14 mm. long, $\frac{1}{2}$ mm. thick; the female, to 25 mm. long, 1 mm. thick. Once found in the parenchyma of the lungs of a boy.

Another variety of strongylus, STRONGYLUS ARMATUS, is the cause of one of the most frequent and most dangerous diseases of the horse, the so-called colic,—aneurism (*wurm aneuryma*) of the arteries supplying the intestines. This aneurism is true and mixed, of the size of a pea to that of a man's head, and is dependent on a traumatic arteritis caused by the worm mentioned; through inflammation the lumen of the vessels is also narrowed, and there is formed for the most part a fixed thrombus, while the muscular coat hypertrophies and the adventitia is indurated and thickened. The thrombus, as such, and emboli from it, give rise to dangerous symptoms: hæmorrhagic infarctions. paralysis of the muscular coat of the intestines with constipation and strong meteorism, rupture of the intestine; by the progress of the disease back along the mesenteric arteries into the aorta, diseases, especially paralysis of the hind extremities. Consult BOLLINGER, *Beitr. zur vergl. Path. u. s. w. der Hausthiere.* 1870 u. 1872.

ANCHYLOSTOMUM DUODENALE, S. STRONGYLUS DUODENALIS.

Body cylindrical. The head turned round to the surface of the back, with a wide mouth and horny mouth-capsules; on the upper border two strong claw-shaped hooks. Bursa three-lobed. The males reach 10 mm. in

length, and 1 mm. in thickness; the female, 18 mm. in length, 1 mm. in thickness. Found in the duodenum and beginning of the jejunum. In Italy, but especially in Egypt and in tropical countries; sometimes singly, sometimes in very great numbers. It bites its way into the mucous membrane, pierces the submucous cellular tissue, and subsists on the blood. After its removal there remains an ecchymosis of the size of a lentil, the centre of which presents a white spot of the size of a pin's head, with a fine hole. Out of these wounds the blood oozes into the intestinal cavity. When the worm is in the submucous cellular tissue, the inner surface of the intestine presents flat elevations of the size of a lentil and of a brownish color. Seldom single, mostly by thousands. It gives rise to anæmia, and the very extended Egyptian chlorosis.

The *Strong. duod.* probably passes its youth in dirty water, and is thence conveyed with the drink immediately into the intestinal canal, where in a few weeks it assumes its definite form.

According to GRIESINGER (*Arch. d. Heilk.*, 1866, p. 381), tropical chlorosis (*geophagia*) is most probably dependent upon the *anchylostomum*.

3. FAM.: TRICHOTRACHELIDÆ.

Moderately large, longitudinally striated worms. The body is for the most part provided with a thin, elongated, neck-like anterior segment. The mouth, small, without papillæ. The penis with a tubular sheath.

TRICHOCEPHALUS DISPAR, LONG THREAD-WORM.

Body short, about 2 cent. long, 1 mm. thick, to which is attached a filiform neck, 20–25 mm. long, and head; in the male, spiral; in the female, straight. The tail is blunt in the male, pointed in the female. The male is lighter colored than the female, the latter being darker from the presence of ova shining through. It is found in children and adults. Often in the cæcum and ascending colon; less often in the lower small intestine. Often found in great numbers. Its effects are unknown.

TRICHINA SPIRALIS, (OWEN.)

Occurs in man in the developed and undeveloped states.

The mature trichina is attenuated at the anterior extremity; at the tail, blunt, rounded. The intestinal canal passes direct through the length of the whole body, and is divisible into œsophagus, stomach, and rectum. Viviparous. The male, 1.5 mm. long; the female, 2–3 mm. The female genitals lie for the most part in two-thirds of the body. The testicles are located in the last third of the body. Found in the small intestine, less often in the large intestine, of man, swine, of the dog, cat, rabbit, guinea-pig, rat, and of isolated birds.

In the immature state the body is filiform, about 1 mm. long, and has, besides the intestinal canal, no internal organs, or, at the most, only rudiments of such. The trichinæ, twice or three times spirally coiled, occupy the voluntary, striated muscular fibres of man and animals, within very small, elliptical or lemon-shaped, thick-walled capsules, which later become calcareous, and inclose, for the most part, one, rarely two, very rarely three worms. In this state they remain for years capable of development.

From an observation by KLOPSCH (trichinosis in 1842, in 1866 second amputation of a recurring mammary cancer), trichinæ occupying the muscles may attain the age of twenty-four years (*Virch. Arch.*, XXXVI. p. 609).

On the second day after the use of raw flesh containing trichinæ, and the consequent entrance of trichinæ into the intestinal canal, and after the digestion of the inclosing capsule, the worm reaches its full sexual maturity. They there copulate, and on the sixth day thereafter the females bring forth, in great numbers (about 1,000), living filamentous embryos. The young immediately (on the tenth day after the use of the trichina-flesh) begin their wandering, pierce the walls of the intestine, and, partly through the abdominal cavity by way of the intermuscular connective tissue, partly with the blood, they reach the voluntary muscles of their bearer. The muscles first affected are those of the body and head, then those of the extremities. They pierce into the interior of the muscle-bundle, and already on the fourteenth day reach the size and organization of living trichinæ, undeveloped, in the muscles. The infected muscle-bundle very soon loses its earlier structure, while the fibrillæ become homogeneous or assume the appearance of a finely granular substance; later the sarcolemma thickens and begins from the end to shrivel, while the parasite coils itself within in a spiral manner, and the inhabited place is enlarged and spindle-shaped. Then, under the thickened sarcolemma the formation of the lemon-shaped or spherical cysts, through hardening and calcification of the horny substance, begins. Simultaneously there arises in the neighborhood of the affected muscle-bundle a cellular growth, which originates in the nuclei of the capillaries themselves and their surrounding tissues, as well as in the nuclei of the muscle. Out of the former are formed new capillaries, as well as a thick capillary network around the trichina-capsule; out of the latter, new muscle-fibres, so that in the greater number of cases a complete regeneration of the muscular tissue occurs.

The trichina disease assumes various forms, especially according to the number of trichinæ taken capable of development. In the severer cases there occur in the first week after the infection, digestive troubles of different degrees. In the second week there arise the quite characteristic group of symptoms in the muscles of the trunk and extremities (feeling of stiffness, hardness, pain from pressure and movement, hoarseness, dyspnœa), fever, continuation of catarrh of the mucous membrane of the stomach, œdema, etc. It ends in recovery, sometimes after a long time, or death. Light cases present no symptoms, or such as are uncharacteristic.

ZENKER with GERLACH regards the hog as the true and original bearer of trichinæ, the true source of trichinæ. Infection of hogs takes place by swallowing intestinal trichinæ and embryos which had been passed with the excrement of other hogs, but especially by eating trichinous flesh of other hogs; also by feeding the refuse flesh at butcheries to the hogs in the yard. Trichinous rats are a sign of the presence of trichinous hogs.

VIRCHOW, *Arch.*, XVIII. p. 330. ZENKER. *Ib.*, XVIII. p. 561; *Jahresber. der Ges. f. Natur-u. Heilk. zu Dresden*. 1861, u. 62, p. 49 u. 53; *D. Arch. f. klin. Med.*, 1871, VIII. p. 387. BÖHLER, *Die Trichinenkr.*, 1863. LEUCKART, *Unters. üb. Trich. Spir.*, 1860. FIEDLER, *Arch. d. Heilk.*, V. p. 1. COLBERG, *Deutsche Klin.*, 1864, No. 19.

4. FAM.: FILARIDÆ.

With very long, filamentous body, sometimes with, sometimes without papillæ.

FILARIA MEDINENSIS, THREAD-WORM, GUINEA-WORM.

Female, 3 cent. to 1 M. long, 2 mm. thick, white, becoming thinner posteriorly; the male, much smaller and little known. Inhabits especially

the subcutaneous cellular tissue of the foot, less often other places (scrotum), and the conjunctiva bulbi. Found only in tropical countries. Lies in the places mentioned, sometimes coiled, sometimes stretched out. Examples of it are found most often singly, sometimes in great numbers. When the brood of the female worm has reached maturity, there arises in the skin a sort of swelling which is perforated; with various local and general symptoms.

The researches of FEDTSCHENKO in Turkestan make the order of life of the young filariæ as follows : The filariæ already in the womb creep out, are some time free in water, then wander into the small fresh-water crabs (*cyclops*), and if these, with dirty drinking water, are consumed by man, he becomes infected.
DRACUNCULUS OCULI. Under the conjunctiva of Æthiopians.
FILARIA LENTIS. In the crystalline lens and liquor Morgagni.
FILARIA HOMINIS S. BRONCHIALIS. In the bronchial glands.

CLASS : ANNELIDÆ, RINGED WORMS.
Cylindrical or flattened worms, mostly with segmented body with brain, œsophageal ring, chain of abdominal ganglia, and bloodvessels.

ORDER : HIRUDINIS, LEECH.
Body with narrow rings, with terminal central disk, without feet, hermaphrodite, and mostly parasitic.

SUB-ORDER : GNATHOBDELLÆ, GILL-LEECH.
Throat provided with three, often dentated gills, longitudinally plaited ; 4 to 5 rings, for the most part, are upon one segment. In front of the mouth is a prominent, curled, spoon-shaped disk, which forms a sort of oral sucker. Its blood is mostly colored red.

HIRUDO, BLOOD-LEECH.
Has usually ninety-five distinct rings. The anterior rings bear ten spots (eyes). The male genital pore lies between the twenty-fourth and twenty-fifth rings ; that of the female, between the twenty-ninth and thirtieth rings. Gills dentate. The stomach, with eleven pairs of lateral pouches.
HIRUDO MEDICINALIS, with its distinct officinal varieties, has eighty to ninety fine teeth on the free border of the gills. Is cultivated in leech-ponds, and needs three years to arrive at sexual maturity.

III. ARTHROPODA.

Laterally symmetrical animals with segmented bodies and articulate appendages (limbs), with brain and abdominal ganglia. Propagation preponderately sexual.

CLASS : ARACHNIDÆ.
Air-breathing arthropods with head and thorax blended, without feelers, with two pairs of jaws and legs, and abdomen without members. Sexes distinct. Mostly oviparous, seldom viviparous.

ORDER : LINGUATULIDÆ, PENTASTOMIDÆ.
Body worm-shaped, elongated, flat or rounded, ringed. Mouth on the anterior end, rounded, open, surrounded by a horny border. Four legs, hook-like, and sheathed. Surface of the body hard and pierced by stigmata. The female genital opening in the tail; that of the male on the abdominal surface. Penis doubled, very long, filiform. The male smaller than the female. Metamorphosis complete.

PENTASTOMUM TÆNIOIDES.

Female 80, male 20 mm. long. Inhabits the nasal cavities and frontal sinuses of the dog and wolf, very seldom those of the horse and goat. The embryos, within the shells of the ova, are expelled with the mucus and adhere to plants, and thence are taken into the stomach of rabbits, hares, goats, man. In man, as well as in all the last-named animals, only the larvæ are found.

PENTASTOMUM DENTICULATUM.

This form is 4–6 mm. long, 1.5 mm. broad, always encapsuled, curved to the shape of a half-moon, calcified. It is often found located on the surface of the liver, seldom in its interior, especially of the left lobe, on the surface of the small intestines, stomach, kidneys, spleen, lungs. Frequent. It is without consequences.

Twice have I found a living, well-formed, but not fully grown, *pent. dent.* in a distinctly prominent recess of the surface of the liver, which recess was of the size of a half-pea, cyst-like, but not smooth, and not provided with an enclosing membrane. At a distance from these were found three calcified pentastoma. Also I found two specimens of well-formed *pent. dent.* on the surface of the lung of a mangy cat; one was completely calcified, the other in the process of calcification.

ORDER : ACARINÆ, MITES.

Body compact, inarticulate ; abdomen blended with the anterior part of the body ; apparatus of mouth for biting, sucking, or stinging ; respiration by means of tracheæ.

FAM. : DERMATOPHILI, HAIR-FOLLICLE MITE.

Elongated little mites, with lengthened, worm-shaped, fringed abdomen, with suckers and stiletto-shaped jaws, and four pairs of short, bipartite stumped feet.

ACARUS FOLLICULORUM, COMEDONE-MITE, (SIMON.) (*Macrogaster platypus, Dermodex folliculorum.*)

A slender animal, about 0.2 mm. long. Organs of generation and development unknown. Very common. Found in most men in the earwax and in the sebaceous glands of the external organs of hearing and of the face, seldom in those of the chin, breast, etc., not in those of the extremities. In most cases, many animals, sometimes even ten to twenty, are found in one follicle. With the exception of occasional comedones and acne-pustules, there are no consequences.

Mites similar to the *acarus follic.* occur also in dogs, cats, sheep, bats, etc.

FAM. : ACARIDÆ, MITES.

Bodies microscopic, compact, soft-skinned, with horny stalks for the support of the limbs. Legs mostly short, stumped, and provided with disks for prehension.

ACARUS, *seu* SARCOPTES SCABIEI, ITCH-MITE.

The female is about 0.5 mm. long, 0.4 mm. broad, dull grayish-white ; the male almost half as large and strong. Body rounded, arched, with shallow indentations and swellings, and fine parallel transverse striæ. On the dorsal surface are numerous conical elevations and spines ; on the back, sides, and

legs, isolated long bristles. Head round, with bristles and mandibles. In the mature state there are eight legs, of which two are situated anteriorly near the head, and are provided with terminal disks ; two pairs are situated posteriorly, and terminate in long strong bristles. The ova are oval, about 0.2 mm. long, and in them the young mites are sometimes seen, which after creeping forth have only one pair of feet posteriorly.

The female itch-mite penetrates the epidermis of the inner side of the fingers and of the wrist, and forms under it a somewhat winding passage, which is colored brownish by dirt and the excrement of the mites. At the end of the canal (cuniculus) it perforates the corium, therein giving off an acrid liquid which excites itching, and, consequently, the skin affection is known as the common itch. In cases of long duration especially, there are not rarely found abundant scales and crusts, the so-called itch-scabs.

According to DELAFOND and BOURGUIGNON, the *sarcoptes hominis* occurs also on the dog, the horse, and lions.
(FÜRSTENBERG. *Die Krätzmilben der Menschen und Thiere.* 1861.
The mites (*sarcoptes* or *dermatodectes?*) accidentally borne by man are : the true *sarcoptes felis, sarc. canis, sarc. equi, sarc. bovis, sarc. ovis.*

FAM. : IXODÆ, TICKS.

Larger, mostly blood-sucking mites, with firm back-shield and large, extended dentated mandibles. They live upon grasses and upon trees of the garden and forest, and only occasionally are they found upon man. The female sinks its proboscis into the skin, fills itself with blood, by which it swells out and causes, besides pain, suppuration of the part affected. There are : *ixodes ricinus*, the common tick ; *ix. marginatus*, the bordered tick ; *ix. americanus humanus.*

The DERMANYSSUS AVIUM, or ARGAS REFLEXUS, is likewise found on man, accidentally or when in want of other subsistence. It lives in dove-cotes, hen-roosts, bird-cages, etc., upon the affected animals. It gives rise to an itching, burning pain, and leaves behind a reddened, somewhat swollen bitten place, sometimes also œdema, etc.

BOSCHULTE (*Virch. Arch.*, XVIII., p. 554) and GERSTÄCKER (*Ib.*, XIX., p. 457.)
The ARGAS PERSICUS likewise appears to belong to this family.

FAM. : TROMBIDIDÆ, RUNNING-MITES.

Body brightly colored, covered with hair. They run upon plants and upon the ground. The young, six-legged, live parasitically upon insects, etc., sometimes also upon man. The so-called LEPTUS AUTUMNALIS, gooseberry or harvest mite, often in great numbers, penetrates the skin of the reapers, etc., in summer, causing troublesome itching, inflammation, and swelling, sometimes even fever. It is easily recognized on account of its reddish color, hence the name of the affection, ROUGET.

(GUDDEN, *Virch. Arch.*, LII., p. 255.)

CLASS : HEXAPODA, INSECTS.

Air-breathing arthropods, whose body generally is distinctly separate into head, thorax, and abdomen, with two feelers on the head, and three pairs of legs on the tripartite thorax.

9

ORDER: RHYNCHOTA.

SUB-ORDER: APTERA.

Small wingless insects, with short, turned-in, fleshy beak, and piercing bristles, or with rudimentary biting mouth, with a body posteriorly composed, usually, of nine articulations.

PEDICULUS CAPITIS, head-louse.
PEDICULUS PUBIS *vel* PHTHIRIUS INGUINALIS, crabs.
PEDICULUS VESTIMENTI, clothes-louse.

In very rare cases there arises the so-called louse-disease, PHTHIRIASIS, in which the clothes-louse is found in ulcers of the skin, and even under the skin in boils and pustules, the covered louse-ulcers, so-called. (LANDOIS, *Wien. med. Wochenschr.*, 1865, Nos. 17–19.)

SUB-ORDER: HEMIPTERA.

CIMEX LECTULARIUS, *Acanthia rotul.* Bed-bugs.

VIRCHOW (*Arch.*, LIV., p. 283) describes an immense invasion of wood-lice (*clothilla inquilina*, v. HEYDEN).

ORDER: DIPTERA.

Insects with sucking and piercing mouth-apparatus, inarticulate thorax, with cuticular anterior wings, swing-bats for wings posteriorly, and complete metamorphosis.

PULEX IRRITANS, flea.
PULEX *vel* DERMATOPHILUS PENETRANS, sand-flea.

The latter lives in South America. It pierces the hairless parts of the epidermis in an oblique direction, and having reached the cutis it deposits numerous ova, whereby the animal formerly appearing as a long brown point, swells out into a pearl-gray vesicle, of the size of a pea. When the ova reach maturity they are expelled, and develop further in the sand. After that the insect dies, and is cast off with the epidermis. The parts of the skin deprived of sensibility, of those affected with leprosy, often show numerous holes caused by the sand-flea.

Of the *Diptera* the following, partly parasitic, are worthy of notice:

ŒSTRUS HOMINIS, gad-fly. It lays its ova in the skin of man, giving rise to boils.

MUSCA VOMITORIA, large, blue-bottle fly.
SARCOPHAGA, common flesh-fly.
MUSCA DOMESTICA, house-fly.

All deposit their ova with the—for the most part already formed—larvæ, or the latter themselves in the cavities of the mucous membranes of the surface (conjunctiva, nasal cavities, vagina), upon excoriated parts, in wounds and ulcers. In rare cases the larvæ enter the stomach, where they remain several days alive, and possibly give rise to intense catarrh of that organ (MESCHEDE, *Virch. Arch.*, 1866, and GERHARDT, *Jen. Ztschr.*, 1867, p. 454). THOMAS (*oral com.*) saw a severe ear-dialgic attack in consequence of a living wasp having entered the stomach; recovery after the escape of the wasp by vomiting.

According to COQUEREL (*Arch. gén.*, 1859, June), a fly (*Lucilia hominivorax*) occurs in Cayenne, whose larvæ gives rise in man to very severe illness and even death. When present in the nasal cavities and frontal sinuses, they cause pain, hæmorrhage, meningitis, etc.

9. CONTAGIONS AND MIASMATA.

EPIDEMICS AND ENDEMICS.

The literature of the subject is found in works on general pathology, on the acute exanthemata, and in Griesinger's "Infectious Diseases" (*Virch. Handb. d. spec. Path. u. Ther.* II., 2 Abth. 2 Aufl., 1864).

The cause of a number of the most important diseases, contagious and miasmatic, is still almost unknown. It is most probably SPECIFIC, and affects the body like a poison, a VIRUS. Although we know only the effects of this unknown agent, we may, nevertheless, suppose for each of these diseases a definite material, because the disease spreads either from individuals already sick in a similar manner, or at certain times, or proceeding from determined localities the disease spreads, and because the cases of disease in the same category, thus arising, behave in an extremely similar manner. Besides, they have much in common with respect to their symptomatology.

The influence of such a virus upon the body we call INFECTION, and the respective diseases receive the name of INFECTIOUS DISEASES. These diseases form a special group, and do not include the affections which are independently produced WITHIN THE BODY ITSELF, by outside influences, by means of transpositions of a kind partly or entirely unknown, although the action of those products of transposition are to the senses in part quite similar to the infecting substances mentioned. Thus tuberculosis, carcinosis, pyæmia, septicæmia, etc., not arising from an exterior cause, are not ranked among the infectious diseases.

In the spreading of these diseases by infection, the locality of origin of the virus varies. When the virus, by which an individual becomes sick, has its origin only within another individual already sick, from whom it is excreted in an active state with the power to spread from individual to individual, then is the disease called CONTAGIOUS, and the unknown material, CONTAGIUM. But if the unknown agent which further propagates the same disease has originated in the ground, and is diffused through the air or water, so that one may become infected without having met another already sick, or so that the sick cannot be the means of the further spread of the disease, then it is called MIASM.

These two expressions for the manner of spreading of individual diseases are with ease kept sharply distinct. Intermittent fever is not contagious. It is well known that one can, with impunity, approach another sick with intermittent fever; but it is also known that a residence in certain places is dangerous, so that the cause must lie in the ground or in the air. Intermittent fever is decidedly and essentially of miasmatic origin. On the other hand, in measles, scarlet fever, small-pox, whooping-cough, diphtheria, epidemic parotitis, as well as in syphilis, the ground and air do not transport these diseases; he only becomes sick with measles who has been near another sick with measles, and he only with syphilis who has come in immediate contact with an individual affected with syphilis. These diseases are of a decidedly contagious nature.

In a wider range of diseases, however, as cholera, typhoid fever, etc., it is not to be decided whether they are propagated in one or the other way, or in both ways. In these diseases both ways of propagation have been observed, and on that account are called MIASMATIC-CONTAGIOUS. It is believed that the poison arising by the disease is developed not only in the body of the sick person itself, but also in the clothes, etc., or in his room, in the privy, in the floor, etc., is developed or multiplied, and only then is received by others. The diseases thus arising are, typhoid fever, cholera, yellow-fever, the plague, hospital-gangrene, dysentery, influenza, pyæmia, and puerperal fever, perhaps also facial erysipelas and cerebro-spinal meningitis. But this assumption has lately been contested.

The acute exanthemata (small-pox, scarlet fever, measles) are exquisitely contagious diseases. But whether, in a place where a great number are taken sick, the separation of the healthy is of service, it is as yet hardly safe to determine, but it is

at the least improbable.   The latter especially is in accordance with the experience
of PANUM in measles (*Virch. Arch.*, 1847, 1., p. 492).   He observed an epidemic of
measles in the Faroe Islands, which raged from April to October in 1846, and which
attacked over 6,000 of the 7782 inhabitants.   For sixty-five years measles had not
been known on those islands, which is explained by the fact that the islands were
almost shut out from the rest of the world by a commercial monopoly, and that the
seventeen inhabited islands and their cantons have very little intercourse with one
another.   PANUM here many times determined that measles only was communicated
by immediate intercourse with those sick of the same disease; in a few cases
indirectly (through the clothes).

In England, since the researches of WILLAN and BRIGHT, erysipelas has been
regarded as a contagious disease.

Typhoid fever and cholera are, according to the common view, CONTAGIO-MIAS-
MATIC diseases.   They spread through those sick with the disease, or by objects
which have been used and have become infected by them: thus they are contagious.
For the first cases of sickness in a community are often those of persons who have
had direct intercourse with the sick.   But very often also they are seized who had
not stood in the least direct relation with the sick, but who live upon the same soil
as the sick, or who had drunk the water infected by the soil; this is miasmatic pro-
pagation.   Then outside nature furnishes the route of the poison from the first sick
person to its new sphere of activity.

Some, especially PETTENKOFER, will not accept the idea of contagio-miasmatic
diseases.   Many of the diseases in question are by P. included among the transport-
able miasmatic diseases, especially cholera, typhoid fever, yellow fever.   These have
their seat not in the human body, as *e.g.* syphilis and small-pox, but in the same local-
ities; they are not a production of the body, but of a certain locality, etc.; their
poison is taken up from their localities like the poison of malaria.   The spread of
cholera in Bavaria, Thüringen, Saxony, etc., shows, according to P., that the epi-
demically affected places of a country are not connected by lines of commerce, but by
drainage and character of the soil.   NOTT has lately shown the same of yellow fever.

According to PETTENKOFER (*Z. f. Biol.*, 1872, VIII., p. 492), small-pox is a much
more contagio-miasmatic disease than cholera, etc.; its varying frequency can-
not be explained merely by the contagium always present, and the change in the
individual disposition of the population.   The infectious material may be propagated
and increase also outside of the organism, in the substrata of the surrounding soil,
i. e., miasmatically.   P. appeals for confirmation especially to the researches of
MACPHERSON (*Cholera in its Home.*   German by VELTEN, 1867).   M. found, that in
small-pox in Calcutta, in twenty-nine November months fewest (132) died; in the
March months most (4,934). that, besides, the difference in the yearly frequency was
almost one hundred times greater in small-pox than in cholera.

PETTENKOFER'S views with respect to typhoid fever are opposed by BIERMER (*Ueb.
Entst. u. Verbreit. d. Abdominaltyphus.*   VOLKM., *Klin. Vortr.*, 1873, No. 53).   Typhoid
fever according to B., is contagious, and is transmissible through the sick and their
linen smeared by their dejections.   It is regenerated in the intestinal canal and spread
through those affected, or multiplies in the soil, in latrines, etc., and spreads thence
through the air, or drinking-water.

Laymen, and even many physicians, still further extend the conception of infec-
tion.   Besides contagious, miasmatic and miasmatic-contagious diseases, they here
include: 1. Many diseases which not infrequently attack several members of a
family, at a more or less fixed period of their lives, and in whom an inheritance cer-
tainly or probably exists: tuberculosis, scrofulosis, cancer, gout, rheumatism, hys-
teria, affections of the mind, etc.   2. Many diseases or appearances of disease, which
arise from a kind of imitation, especially in children and women: gaping, coughing,
(whooping-cough?), convulsions, etc.   3. The so-called parasites, animal and vege-
table.   4. The zoonoses, so-called (madness, hydrophobia—gangrene of the spleen,
and carbuncles, anthrax and malignant pustule—glanders and farcy, *malleus humidus
et farciminosus*), in which there is a transference between individuals of different
species, and for the most part from animals to man.   5. The so-called purulent-con-
tagious diseases, *i.e.* those contagious affections in which pus is the bearer of the
contagium, which adheres only to certain organs, and always gives rise to only local
difficulties (gonorrhœa, ophthalmia of the new-born, Egyptian ophthalmia).

BOUCHUT (*Wien. Wochenschr.*, 1861, Nr. 43) and REMAK (*Med. Central-Ztg.*,
1864, Nr. 87) add to the present number still a NERVOUS CONTAGIUM, which should
explain the spread of certain diseases of the nervous system, *e.g.* chorea, hysteria,
epilepsy, diseases of the mind.   According to VINGTRINIER, TOURDES, etc., a miasm
similar to that of intermittent fever is the cause of endemic goitre, which miasm

VEST calls *bronchin*. It is distributed sometimes with the water of a region, sometimes with the air, sometimes with both.

The INFECTING AGENT, the specific poison, is not certainly known in any contagious or miasmatic disease. Various theories have been brought forward concerning the nature of this poison. Of these the so-called parasitic theory has found almost universal acceptance; it is at least the most probable. But investigations carried on for the last ten years, are, in spite of all the declarations of observers, not yet so far removed from doubt, that the assumption of a so-called *contagium animatum* can be regarded as assured. Formerly, infectious diseases were regarded as the working of purely chemical gaseous products: so-called fermentation or zymotic diseases. Many phenomena, especially contagion, are explained much more simply by the parasitic theory than by a chemical theory. Therefore gaseous substances may yet always be influential as auxiliary causes of infection. Thus *e.g.* sewer-gases, contaminated well-water, etc.

On the other hand, in a few especially contagious affections, the bearers, vehicles, of the *contagium* are known. In syphilis it lies in the pus of the ulcers; in small-pox in the serous fluid, which is found in the vesicles before the development of pustules; in measles probably in the tears, in the secretion of the air-passages and in the serous contents of little vesicles, etc. These fluids, *e.g.*, have been inoculated, *i.e.* introduced under the skin of healthy men and animals near the bloodvessels; thereafter the same local and general symptoms have appeared in the same succession, and with tolerable regularity, as in the one from whom the virus had been taken. The vehicles of the miasmatic diseases are not at all known; those of the miasmatic-contagious affections only partially. Of cholera, typhoid fever, and dysentery, the dejections, and consequently the linen, bedding, night-vessels, syringes, etc., may be the bearers of the contagium. The same is true of diphtheria. Here the deposits on the mucous membrane of the palate and throat are infectious.

Syphilitic pus, the tears of those sick with measles, etc., have been examined in every way, chemically and microscopically, and no difference has been found to exist between syphilitic pus and non-syphilitic pus, which, inoculated, communicates no infection, etc. These substances have been exposed to heat and cold, and have been treated with corrosive sublimate, chlorine, alkalies, etc.: their power to infect ceases when the organic materials have been destroyed.

According to CHAUVEAU (*Compt. rend.* 1871, LXXIII., No. 2) the poisonous substance in contagious liquids is not dissolved, but, as also in the air, is suspended in form of small particles.

The mode of origin of contagions is unknown, and probably differs in different cases. Of many contagions it has been assumed that they have only once been generated, and afterwards have been propagated from individual to individual, or that in very rare instances they had been generated anew: so-called permanent contagions, *contagia communicativa, e. g.* small-pox, syphilis, measles, cholera. Of others many believe that they always arise anew (scarlet fever, and exanthematous typhus, and typhoid fever), but then spread epi- or endemically. This assumption is, however, not necessary to the explanation of the phenomena. The mode of origin of miasmata is likewise little known.

Contagious have a certain duration, as well as the ability to act near by and at greater distances. The duration of the material of infection has

been denoted by the term *tenacity*, in so far as it adheres for a length of time to its bearers. Lymph from cow-pox can be kept in a dried state for a year and longer without losing its power to infect when inoculated. This tenacity appears to be longer preserved by the receiver being kept from the air. In exanthematous typhus it has been observed that in rooms in which those affected with the disease had lain, and which had stood empty for more than seven months, the next occupants were affected with the same disease. The same has been observed of cholera.

With respect to the manner of propagation, contagions are distinguished as fixed and transient (*contagia fixa vel per contactum*, and *contagia halituosa vel febrilia*). In the former are those substances which are the media of infection, the so-called vehicles of contagion, fluid or more or less solid (pus, etc.); in the latter, gaseous bodies (expired air, perspiratory vapors). The former act only by immediate contact or by inoculation of the peculiar product of disease; the latter, directly or indirectly, at a greater or less distance.

Fixed contagions are found, especially in syphilis, which become contagious only by the most immediate contact with the similarly sick; in the same manner, also, by inoculation with syphilitic pus,—in both cases only by wounding the skin or mucous membranes. The contagions of measles, scarlet fever, small-pox, whooping-cough, cholera, and of exanthematous typhus, are transient.

In what concentration of the contagion, and at what distance infection follows, is questionable. Usually a short stay in the sick-room is sufficient; or even in the adjoining rooms, in measles, small-pox, probably typhus fever, and cholera. In other diseases sometimes only a short stay in the sick-room is necessary for infection, sometimes the latter results only after longer contact with the sick (exanthematous and abdominal typhus, by which physicians and nurses especially are attacked).

A mother can convey an infectious disease, *e.g.* variola, to the fœtus she bears, without being affected by the disease herself.

With respect to diphtheria there are many mysterious circumstances. According to BARTELS (*D. Arch. f. klin. Med.*, 1867, i. p. 367), its spread does not result like that of the acute exanthemata from the transmission of a contagion from person to person, or it is at the least in this manner wholly exceptional. In hospital B. has never seen an instance in which the contagion had been communicated to an occupant of a neighboring bed or room. On the other hand, the most striking circumstance is the persistence of the disease in localities, which likewise distinguishes it from the acute exanthemata.

Doubtless in transient contagions a mediate infection is also possible, *i.e.* through substances which had been used by the sick (clothes, linen, beds, furs, etc.).

In several of PANUM's examples the contagion of measles had been conveyed from a distance in clothes which had been worn by people who were themselves not susceptible of the contagion, once after traveling a distance of four miles in an open boat in stormy and rainy weather. The same has been observed in small-pox, cholera, typhoid fever, scarlatina. Cholera and typhoid fever are more surely infectious if their dejections have been for a long time exposed to the air. dried in the linen, etc.: hence the frequency of sickness of washerwomen, etc. This is of importance, on the one hand, because the physician can become the means of transmitting the infection ; on the other hand, with respect to measures in general for protection. It has also been justly asserted that puerperal fever can be transmitted to a lying-in woman from one suffering from that disease, by healthy persons (midwives and physicians).

Individual contagious diseases (*e.g.* the common chicken-pox) have a fixed and transient contagion. The inoculability of measles (HOME, SPERANZA, CATONA, MAYR), and of scarlet fever (G. SIMON) has not yet been certainly demonstrated.

The reception of contagions takes place, according as they are fixed or transient, either through the skin and adjacent mucous membranes, or through the lungs.

Infection takes place through the skin and mucous membranes in syphilis, cow-pox and small-pox ; in the former, accidentally or by experiment ; in the second, purposely by inoculation ; in the third in the same manner, although now no longer practised. Whether an accidental or experimental wound of the skin, and especially of the mucous membrane, is in all cases necessary, is questionable in syphilis and cow-pox, but very probable. Infection takes place through the lungs, perhaps also through other mucous membranes and the skin, in measles, scarlet fever, small-pox, whooping-cough, cholera, typhoid fever ; the exhalations being direct from the sick, as well as mediate from the clothes, etc.

Many contagions are probably received at one time by the organs of respiration, at another time by those of digestion (drinking-water); *e.g.* that of typhoid fever.

KÜCHENMEISTER kept a sheep for an hour in a sack with a shirt which a person sick with small-pox had worn, the pock being then in the stage of umbilicated vesicle. The sheep lost its desire for food, etc., on the fifth day, and on the eighth day there appeared a well-marked eruption on the inner surface of the upper part of the thigh.

Concerning meat and milk as bearers of the infectious matter of tuberculosis, *vide infra.*

Concerning milk as a vehicle of the infectious matter of typhoid fever, consult BALLARD (*On a Local Outbreak of Typhoid Fever in Islington, traced to the Use of Impure Milk.* London, 1871).

While with respect to contagions it is assumed that they act by means of an exceedingly small quantity of infectious material, a certain quantity of it is held to be necessary in miasmatic-contagious and purely miasmatic diseases, and it is believed that the latter are dependent upon the quantity of this material. On this account miasmatic-contagious and miasmatic diseases spread, especially when the miasm accumulates in the so-called foci of infection, *e.g.* by crowding the sick in close, badly-ventilated localities, by privies, etc.

These considerations are of importance with respect to quarantine, which in contagious diseases (*e.g.* measles, small-pox, also yellow fever and cholera) is of the highest service, indeed often furnishes absolute security, but, on the contrary, in miasmatic diseases is injurious.

In what stage of contagious disease the contagion is generated, *i.e.* when the infection has reached its greatest power, is only imperfectly known : in the acute exanthemata before and during the eruptive stage, in typhoid fever and cholera probably during the period of profuse diarrhœa.

In measles, infection reaches its greatest power during the eruptive stage and the stage of efflorescence, while during the period of incubation and during the prodromal stage and that of desquamation, especially the former, the disease cannot spread. In cow-pox the lymph is most active from the sixth to the ninth day. The duration of activity is much longer with proper preservation. Small-pox and syphilis are infectious as long as pus is secreted in their pustules or ulcers. In what stages of the miasmatic-contagious diseases infection is most powerful, is not yet known ; in individual diseases, probably during the period of active diarrhœa or of diarrhœa generally (cholera, dysentery, typhoid fever). With respect to cholera, it is certain that not merely those sick with cholera, but those suffering from a choleraic diarrhœa and not prevented thereby from going about, traveling, etc., can protract the disease. They do not need even later to have cholera proper, while those infected may become sick with the fully-formed disease. Especially is this shown where, without the least intercourse with the sick, they have taken cholera who had handled and washed linen smeared with choleraic dejections; and where a person afflicted with choleraic diarrhœa leaves cholera in the house in which he had passed the night, or a much shorter time. (PETTENKOFER).

In most cases of contagious or miasmatic disease the specific poison does not suffice to bring forth the disease, but there must be causes to assist the poison in reaching its development and full effect. In individual contagious diseases these auxiliary causes may be wanting, *e.g.* in measles and syphilis. In others, on the contrary, they are essential : as in cholera and yellow fever. These auxiliary causes are partly local (*e.g.* the soil, fluctuations in the ground-water, various relations of privies) ; they are partly dependent on the season of the year (quantity of atmospheric precipitation).

GRIESINGER first distinguished in cholera the specific causes, capable of spreading from one place to another, the cholera poison, and the auxiliary causes, *i.e.* those forces which promote and advance the operation of the poison. Consult also the remarks below respecting epidemics.

Contagious, miasmatic, and miasmatic-contagious diseases exhibit a number of modifications, which with equal clearness and independence do not belong to other and non-infectious diseases. These modifications relate to greater or lesser epidemic or endemic propagation, to the intensity and severity of individual cases of disease (mild or malignant measles, scarlet fever, and diphtheria ; abortive typhoid fever, light and severe forms of exanthematous typhus and typhoid fever), to a sort of exclusion, or inversely, to alternating occurrence, etc. They are especially found in all imperfectly developed infectious diseases, the abortive cases, so-called. These modifications are most prominent in small-pox (*variola vera* and *varioloid*), in scarlet fever, diphtheria, and typhoid fever.

Varicella, regarded by some, especially HEBRA, as a modification of variola, is determined to be an independent disease (THOMAS, VETTER). Analogous conditions probably occur also between diphtheria and many like affections of the throat.

In every case an especial INDIVIDUAL DISPOSITION is necessary for the breaking out of the disease. This disposition, for many diseases, *e.g.* measles and small-pox, is a general one. Individuals are rarely found who, in spite of contact with the contagion, remain exempt, without a reason for it. In other affections the disposition is, from as unknown causes, much less, as in cholera, typhoid fever, scarlet fever.

It is not yet determined whether certain kinds of employment do not grant immunity from many diseases. Statistics relative to this point are to be received with great caution, since immunity often depends upon quite other circumstances than the want of a specific individual disposition.

Healthy and strong people are attacked more often by infectious diseases than the weak, sickly, and convalescent (with the exception of exanthematous typhus). It is not to be concluded from this that weakly and sickly persons do not die more easily when they are once taken sick. In other diseases the difference is not perceptible, or the inverse appears. With respect to age, more often the first year of life and partly the oldest age are more or less exempt from infection, while in these years also typhus fever and syphilis readily occur.

Typhoid fever is seldom found in very young and very old individuals, most often between the fifteenth and thirtieth year. Scarlet fever is almost confined to childhood ; it at times attacks young adults, rarely older persons. The same holds true of diphtheria. True varicella occurs, as it seems, only in children, chiefly young children ; in older children the disposition to it appears to have been lost.

A single attack of the disease, in many contagions, affords almost complete security from another attack : small-pox, measles, scarlet fever, whooping-cough, yellow fever, perhaps also syphilis. In frequent epidemics of these diseases, only those of the population become affected whose birth dates after the occurrence of the last epidemic ; in the remainder, the disposition has been eradicated by a previous attack of the disease. It is so especially in measles.

According to PANUM, of the 6,000 sick with measles in the Faroe Islands, not a person was attacked a second time. Ninety-eight old people who had had measles in their youth, remained exempt. In the epidemic of yellow fever at Gibraltar, in 1828, of the 9,000 sick there was not a well-authenticated case of second attack. Only in recurrent fever, two or more attacks not infrequently occurs. In scarlet fever and small-pox this likewise occurs but rarely.

Two similar, or different forms of contagion may appear at the same time in one and the same individual : cow-pox and measles, scarlet fever and measles, typhoid fever and cholera, chicken-pox and scarlet fever, typhoid fever and malaria, measles and malaria, variola vera and cow-pox. The susceptibility to a contagion is destroyed by inoculation with a modification of the same contagion : small-pox, syphilis.

The EVENT OF INFECTION is very seldom accompanied by special subjective or objective symptoms. In individual severe attacks, many have observed in themselves vertigo, loss of strength, chills, nausea.

Between the time of infection and the first outbreak of the disease proper, is a stage in which, in most cases, the attacked act like healthy persons and feel well—in rare cases, symptoms of general prostration appear : the STAGE OF LATENCY, OR OF INCUBATION. The duration of this stage varies in different diseases ; besides, in a few only, is it exactly known. The knowledge of this period is of great practical importance.

In measles the duration of incubation is usually from 9 to 11 days, seldom longer, to the beginning of the typical fever. According to BÄRENSPRUNG (Annalen der Charité, 1860, IX., p. 103), small-pox has the same period of incubation. The incubative period of yellow fever may be only of one day's duration, or it may extend to several days, or even to three weeks. That the period of incubation of cholera lasts at least one week, is shown when sailors have first become sick with cholera seven days after leaving sea-port towns in which cholera was present. Usually, however, it lasts longer, for the most part two, even three weeks, and longer. (Consult PETTENKOFER, Ueber Cholera auf Schiffen und den Zweck der Quarantainen. D. Vtljschr. f. öff. Gesundheitspflege, 1872, IV., p. 1.) The period of incubation of typhus fever lasts about eight days. According to some observations of BARTELS and others, the incubative period of diphtheria (or croup) occupies three days—at least in cases arising exceptionally through contagion. In syphilis, where the cases are those of soft chancre, there is probably no incubation ; but in cases of hard chancre there is a probable incubation of 28 days (BÄRENSPRUNG, etc.).

The period of incubation is, furthermore, different, according to the way by which the poison enters the body : thus in vaccina and variola ; perhaps also in typhoid fever.

The INOCULATION of certain contagious diseases deserves special mention. It is naturally only possible in those which have a fixed material of infection (measles, small-pox, diphtheria, syphilis, plague). It is not only theoretically, but also practically of the greatest importance.

Inoculation against small-pox, as is known, has been employed since the time of JENNER only as a means of individual protection. It is nowadays no longer done by transporting the contents of the pustules of variola vera, but always by using the lymph of vaccina, or cow-pox.

Whether by the general introduction and legally ordered cow-pox inoculation, other contagions, as syphilis, can also be communicated with it, a question proposed by a general board of health has called forth various opinions. VIENNOIS (*Arch. gén. de méd.* 1860, June, July, September) reached the following conclusions: If a person be vaccinated with clean, pure vaccine matter unmixed with blood, from a syphilitic person, nothing but cow-pox results, without earlier or later syphilitic complication. If, on the contrary, in the act of vaccinating a healthy individual with vaccine matter from a syphilitic person, whether constitutional symptoms be present or not, the point of the lancet becomes spotted with blood, then both diseases can be transmitted : vaccina with the vaccine matter, and syphilis with the syphilitic blood.   In these cases vaccina is developed first, because it has a shorter stage of incubation and a quicker development ; the latter appears later, and reveals itself at the point of vaccination.   An ulcer appears here with hard borders and manifold glandular swellings.

During the last ten years many striking examples have occurred of transmission of syphilis by vaccination. In Rivalta in Sardinia, within six weeks, of sixty-three children vaccinated forty-six became syphilitic through the use of impure lymph (*Gaz. med. Ital.*, 4 Nov., 1861).   A similar thing happened in Hungary (GLATTER in *Œstr. Ztschr. f. prakt. Heilk.*, 1862, Nr. 4) : the grandmother of a child, from whom the others were vaccinated, a midwife, was syphilitic.   In the children which were vaccinated the cow-pox passed into phagedenic ulcers, followed by the appearance of condylomata around the anus and by affections of the mouth.   Farther on, the mothers, and finally the fathers, became syphilitic, so that two years later, in a region numbering 650 inhabitants, seventy-two were syphilitic.

Experimentation by inoculation with the blood or secretions, especially the dejecta, of those sick with cholera, has as yet furnished no decided results. On the other hand, it appears certain that animals which had eaten the excreta of cholera, not infrequently, on that account, sickened and died (LINDSAY, THIERSCH, J. MEYER).

The same theoretical and, in part, practical importance has of late attached itself to inoculation also in syphilis. With reference to the former, the two syphilitic poisons have been used : inoculation with the secretion of a hard chancre succeeds only in healthy individuals, not in those who already have a hard chancre or secondary syphilis, and gives rise to pustules, and subsequent secondary syphilis ; on the other hand, inoculation of the secretion of soft chancre succeeds also in individuals with hard chancres or with secondary syphilis : it gives rise to only local symptoms, at the most to inflammation of the lymphatic glands, never to secondary syphilis.   In soft chancre the incubation period is very short, in the hard variety its duration is about one month. ·   This similarity between vaccine and soft chancre on the one hand, and between variola and hard chancre on the other, as well as many other relations not here discussed, affords a reason for the inoculation of syphilis, not merely on theoretical and diagnostic grounds, but also for the purpose of cure : either to cure only, or, indeed, for the purpose of preservative or preventive syphilization (AUZIAS-TURENNE, MARCHAL DE CALVI, SPERINO, BOECK).   The former was tried only with the syphilitic, while the latter should be extended to all men to prevent primary and secondary syphilis.

BRETONNEAU, HERPIN, and others include diphtheria also among the inoculable diseases.   And yet the practice of inoculation would be of no value, since diphtheria can attack the same individual several times, and since inoculation does not ensure a mild grade of the disease.

In measles and scarlet fever inoculation has, until now, been undertaken only for theoretical, not for practical reasons.   The inoculated disease was much lighter than that occurring in the usual manner.

The special symptomatology of infectious diseases belongs to special pathology.   In general the symptoms begin in contagious diseases, sometimes at the point of reception of the contagium (pain, redness, exudation), sometimes as a general sickness. All diseases of this class are accompanied partly by high fever, partly by affections of definite tissues and organs, especially of the skin and mucous membranes (contagious diseases), as well as of glandular organs, and copious evacuations, or by both.   The course also of most febrile contagious and miasmatic diseases is much more regular than in other diseases ; in all acute febrile infectious diseases it is stamped with a cyclical character.

With respect to contagions and miasms, their GEOGRAPHICAL DISTRIBUTION, as well as the influence which social relations exert upon their occurrence, are of great importance. All these circumstances are important, because they furnish information concerning the possible nature and cause of origin, especially of miasmatic and miasmatic-contagious diseases.

Acute contagious diseases are, as it seems, spread over the whole earth, and independently of circumstances of race, climate, soil, etc. The geographical distribution of small-pox is essentially dependent upon the extent to which vaccination is practised. Diphtheria more often occurs in damp and swampy localities. Many miasmatic-contagious diseases, e.g. yellow fever, cholera, typhoid fever, are more or less dependent upon the circumstances already alluded to. Thus, e.g. cholera, also typhoid fever, arise upon a porous (alluvial) soil, and apparent exceptions are explained by the fact that the rocky substance of a locality is not compact, or is covered by a surface of porous soil. Cholera spreads preferably along the banks of rivers; yellow fever, only on the coasts or banks of great navigable streams. Miasmatic malarial fevers predominate on plains, their intensity and propagation being proportionate to the moisture of the soil and its readiness to dry, also to its varying moisture.

The influence of the TEMPERATURE OF THE AIR upon contagions, and especially upon miasmatic and miasmatic-contagious diseases, is of great importance. Thus, amongst us, malarial fever appears in the spring and early summer; typhus and typhoid, in late summer and autumn; cholera, particularly in summer. The influence of the seasons corresponds in part with the temperature, and yet in the estimate the moisture of the soil and of the air are of the greatest consequence. Thus especially in cholera, typhoid fever, and intermittent fever.

RACE AND NATIONALITY have a decided influence on certain miasmatic-contagious diseases. Especially noteworthy is the almost complete immunity of the negro, and, in a less degree, of the mulatto from yellow fever. This immunity is in part certainly dependent upon acclimation, since a long residence in cold regions makes the negro also susceptible to the disease.

The INFLUENCE OF ACCLIMATION upon the miasmatic-contagious diseases is shown in high degree in yellow fever. This disease occurs, in those regions where it prevails endemically, almost exclusively among those of short residence or the unacclimated; while, on the other hand, the natives are almost entirely exempt. In influenza a complete exemption has often been observed in the unacclimated. The opposite has been observed in cholera, e.g. in Calcutta.

The INFLUENCE OF SOCIAL RELATIONS on contagious diseases is small—if that protection is excluded which the wealthy can provide themselves with by a change of residence, or by complete isolation from the localities of the epidemic, by vaccination in small-pox, and by the various measures employed against syphilis. That influence, however, is, in most miasmatic-contagious diseases, an altogether superior one. Also if the susceptibility to these diseases is, on the whole, a general one, then are individuals in unfavorable circumstances, etc., especially concerned. Thus yellow fever prevails almost exclusively in places with a crowded population, especially in populous cities, while the country people and even those of the immediate neighborhood of the cities are exempt. It occurs especially in dirty, badly-ventilated, damp, narrow streets, and which are covered with animal excreta, with high houses, and densely inhabited with a poor population. Or, here it spreads farther, is more malignant, and remains longer. Cholera attacks preferably the poor, needy, and struggling part of the population, the wealthy classes participating to a proportionately small extent, except in the severest epidemics. Typhus fever has so increased among the Irish people that all sanitary measures have until now been insufficient to exterminate it, or to prevent its developing increasing force, so that it clings to the Irish emigrant as a curse, and follows him everywhere, wherever he takes with him the habitual evils of the life of the lower classes of his home. Social evils (war, failure of crops, famine) are in typhus and typhoid fevers, especially the former, of great influence. Especially is this true of Ireland, where typhus fever regularly appears after failure of the crops. Thence it extends into the English and Scottish cities, where the lodging-houses of the Irish and their dirty huts are crowded together, in which the disease never dies out, and from which, under favorable circumstances, it radiates to a variable extent into the neighboring localities. A similar state of affairs is found in Italy, in Poland, and Upper Silesia, in the Baltic provinces of Russia, and in certain districts of North-west Germany.* The same

* Typhus fever has occurred in the principal cities of the United States (especially along the seaboard) at various times during the past forty years.—ED.]

social conditions were found in the small epidemics in Berlin, Halle, Leipzig, etc. ; among the troops of the western powers during the Crimean war ; and in isolated localities, as prisons, hospitals, institutions for the poor, etc. Typhoid fever also is observed especially often in damp, narrow, dirty streets and houses, in an atmosphere rendered pestiferous by all kinds of effluvia, in over-populated, old, half-fallen dwellings ; occurring sporadically and epidemically. It occurs decidedly more often in large, over-populous cities than in the level country. It concerns in a special manner the immigrant after a few months' residence : the so-called acclimation fever. During the last ten years several instances have been communicated where it has attacked whole streets or portions of a city, etc., in consequence of the water supply rendered impure by infectious filth. Social evils have had the same essential influence on the Oriental plague.

An important peculiarity of contagious and miasmatic diseases consists in this, that many appear almost entirely in a sporadic manner, while others are at the same time and essentially epidemic and endemic. Those diseases are called SPORADIC which attack individuals independently of time and place. On the other hand, those diseases are called EPIDEMIC which attack a number of persons at the same time, *i.e.* on the same day, within the same week or month, and in the same manner. If the pestilence spread over a whole country, or, at the same time, through a whole population, it is called PANDEMIC. If, finally, the same disease be often repeated in one locality, it is called ENDEMIC.

The essential cause of EPIDEMIC DISEASES is partly unknown (*e.g.* contagions and miasms) and partly known. But we must not claim that in every epidemic its essential causal condition can be with certainty established.

The cause, for example, is known of the epidemics of trichinosis which have lately excited so much investigation ; which cause, as far as its spread has been observed to occur in a certain locality, has been termed endemic. More or less known also is the cause, by cold, etc., of rheumatism, pneumonia, erysipelas, whose appearance is rightly called epidemic when they affect a large number. The cause of many epidemics of typhoid fever is likewise known.

Every epidemic shows a period of increase, of full development or height, and of abatement. In most cases the increase is rapid, the height is soon reached, while the stage of abatement is somewhat prolonged. After its departure the disease leaves no traces, not infrequently disappearing entirely for many years, until isolated cases suddenly announce the beginning again of a new epidemic ; or, during the pause it may exist in single, unconnected cases, sporadically. The former way is that of cholera, usually measles also ; the latter, that of scarlet fever, especially in large communities, as well as of small-pox.

The duration of epidemics proper varies greatly, usually not less than from two to three months, and seldom exceeding a half year. In those diseases which are at the same time endemic, the duration is longer and their return frequent and almost regular yearly. In general, the duration of epidemics is longer in large communities than in smaller localities, because of the numerous points of contact of the cause of the disease with individuals capable of infection. This applies to miasmatic affections, so-called, but in an especial manner to those of a contagious nature. The duration is short in epidemics, *e.g.* of measles and cholera, longer in scarlet fever, small-pox, and typhoid fever.

The greater number of epidemic diseases are constitutional ; only a few are local troubles. Among the former are found, *e.g.*, all infections dis-

eases, as typhoid fever, cholera, acute exanthemata, malarious diseases. Fever is present in most affections which appear epidemically.

The spread of an epidemic takes place in several ways, according as the disease is contagious, or is not contagious. In the first instance there are, often under the influence of local circumstances, numerous single, more or less considerable foci of contagion from which the disease again takes its departure. Thus are distinguished the epidemics of streets, houses and rooms. The disease prevails sometimes toward the end of an epidemic in a part of a locality altogether different from that in which it began. In the second instance, the individual cases are scattered about in the affected population without such order.

An epidemic exists in one community only, or in a few neighboring communities, but in its greater extension, over a whole land, it is called a PANDEMIC. Pandemic extension is often seen in cholera, malarious diseases, sometimes in typhous diseases, diphtheria. A pandemic is always made up of numerous separate, large and not contemporaneous epidemics; its duration, therefore, is various, but is for the most part very long, often extending over many years.

The IMMEDIATE CAUSE of the epidemic spread of many diseases is almost wholly unknown. A few arise in abnormal circumstances of the weather, e.g. bronchitis and pneumonia in seasons with frequent raw winds, troubles of the digestive organs during great heat. In the general extension of the influences which cause sickness can be found the cause of numerous cases of disease. Again, an altogether similar weather may exist at other times, and yet diseases of that kind do not appear in greater number. There must also be something present which is essentially concerned in the origin of the affection. Other diseases, e.g. measles, generally attack only once, the individual permeated by the contagion being free. In great extensions of epidemics of measles, there remain, after the departure of the disease, only a few individuals who have not been exposed to the cause of measles. The number of these increases in the following years by means of births, and thus there is at last an abundant material for a new epidemic. Why it appears at one time, and not a few months or a half year earlier or later, it is impossible to say. Still more remarkable is the growth into an epidemic of other diseases, e.g. cholera. Here the germ has often been conveyed into a healthy population for months without especial consequences, until suddenly the epidemic breaks out and runs its usual course, while in other localities it immediately follows the first case.

From such observations it follows that not only the causes of disease and the individuals to be affected are necessary to the rise of an epidemic, but also that there are necessarily other and auxiliary causes. These latter partly influence the causes of disease, partly the individuals, partly, and at the same time, both. The former appear to increase and spread by the agency of auxiliary causes, while in individuals a change of the constitution hitherto unknown precedes, in consequence of which operation of the cause of the disease is possible. Such an assisting cause we rightly assume to exist, for example, in the water from the soil for typhoid fever.

For the development of an epidemic of cholera there must be, according to PETTENKOFER: 1. An inhabited soil permeable to water and air to the depth of the underground-water. 2. A fluctuation in the moisture of this stratum, which, in the alluvium, corresponds to the varying state of the underground-water, during which the time of the falling from an unusual height marks the time of danger. 3. The presence of organic matters, especially those having their origin in excrement, which matters have been diffused in the stratum of the soil susceptible of it. 4. The

specific germ propagated by human intercourse, the specific cause of cholera, the chief bearer of which is the intestinal excrement of those sick with choleraic diarrhœa and possibly also of the healthy who come from localities infected by cholera. 5. A disposition of individuals to become sick with cholera. This view of PETTENKOFER'S has recently found many opponents (BIERMER, SANDER, and others).

BUHL has shown that at Munich a sinking of the soil water is attended with an increase in the number of those sick with typhoid fever ; its rise, with a diminution in the number of those cases. This he explains in this way : by the sinking of the soil-water the strata of the ground apt for the generation of the immediate cause of the fever comes in contact with the air of the surface, through which air the inhabitants of the city are brought in contact with those causes, while by the rise of the soil-water the contrary takes place. VIRCHOW has shown the same for Berlin with respect to typhoid fever.

Typhus fever, recurrent fever, cholera, are, furthermore, diseases especially affecting the poor, while measles and scarlet fever affect equally the rich and the poor. Hence it appears that peculiarities may be generated within the body through favorable and unfavorable external circumstances, which are essentially concerned in the question of origin of sporadic, and especially also of epidemic diseases.

As little is known concerning the origin of epidemics, so also do we know little concerning the causes of the considerable fluctuations during the climax and stage of decline, and of the causes of various degrees of intensity of the same disease in the course of a single year. It not infrequently happens, that certain days exert an unfavorable influence by their extreme temperature and extreme fluctuations of temperature, or by other circumstances of the weather, e. g. violent rain-storms or thunder-storms, while altogether similar circumstances on other days are observed to be without influence, or are effective in an apparently opposite manner. With respect to this nothing certain has to the present time been offered. Similar relations with respect to the course in individual cases are, however, also restricted, since other and more or less complicated forces always come into the account. Thus, e. g., the influence of the season of the year, the influence of a hypothetical qualitative difference (energy) of the specific cause of disease, of the different constitutions of individuals, the influence of certain prophylactic measures, etc.

The EXTENSION OF EPIDEMICS sometimes fluctuates in a very considerable and apparently capricious manner. This is seen most strikingly in the various local epidemics of cholera. Measles sometimes appears in a very inconsiderable epidemic, to appear again after an unusually short interval so much the more violent. More explicable is the very variable intensity of epidemics of intermittent fever, which are here determined by the quantity of moisture in the soil. An explanation of the different intensities is in any case to be found in the circumstance, that for the production of an epidemic, not only one but several assisting causes acting in the most various manner are necessary, that these exist at the same time, although not necessarily so.

The MORTALITY of epidemic diseases is as changing as their spread. In some epidemics all cases recover, in others the percentage of deaths is very considerable, and, too, without any definite perceptible cause for the difference. Thus it is especially in scarlet fever. Some authors have attempted to explain this by assuming a double cause for the sickness, assuming a malignant and an innoxious form ; nevertheless, they have not yet been able to say why sometimes the one form prevails, and at other times the other form. Perhaps malignant epidemics are to be explained by the

simultaneous presence of unfavorable influences and specific material, which affect in an effective injurious manner those sick through the prevailing epidemic. Sometimes a marked spread and often also mortality in certain epidemic diseases (scarlet-fever, diphtheria, typhoid fever) are confined to single families.

Usually they are the most severely sick, most frequently killed, who are attacked during the first half of the epidemic; later, there is an abatement of the intensity of the symptoms of the disease. And yet, indeed, very severe cases not infrequently appear, like stragglers of an epidemic.

Many, or at least two, epidemics can prevail at the same time and possess a tolerable intensity; thus, *e.g.*, scarlet fever and measles, chiefly the acute exanthemata, cholera and typhoid fever, cholera and intermittent fever, whooping-cough and bronchitis. At other times, for unknown reasons, other epidemic or non-epidemic diseases disappear during the prevalence of a single specially extended epidemic, to reappear again after the departure of the epidemic. The tendency of a population to become sick seems in a certain measure to be destroyed by a great epidemic, for not infrequently after its departure there exists a good condition of health for a long time. It is true that in murderous epidemics (*e.g.* cholera) this may depend upon the fact that many sick persons have been swept away.

As has already been intimated above, the PROGNOSIS of epidemics of one and the same disease may be very different. And not only temporarily can a considerable difference arise, but it is often found also in epidemics which are contemporaneous, but affecting different localities. It has been observed, especially in measles, that the disease in larger places which have more frequent epidemics, runs a milder course than in smaller places, in which it appears less often.

PROPHYLAXIS is of the greatest importance in epidemics. The aim of adopting public measures with respect to this, is, on the one hand, to increase the ability of the people to resist injurious causes of disease; on the other hand, to destroy them and render them harmless. This end is reached by cleaning and ventilating places of abode and their surroundings, by procuring good drinking-water, by supplying the poor with food and clothing, by disinfecting sick-rooms and the linen of the sick, by rendering innoxious the dejecta which are often the bearers of the causes of sickness, by removing the sick from their unfavorable dwellings into properly managed public hospitals, by separating the healthy from the neighborhood of the foci of infection and by destroying such foci, etc.

ENDEMICS, under which form diseases partly acute and partly chronic appear, depend upon local peculiarities, which sometimes are the character of the soil, sometimes local regulations and customs, sometimes they result from a certain abnormal quality of the food of the community. Finally, there are endemics which arise from no known causes. Endemic diseases appear partly sporadically, and sometimes sporadically and epidemically. The tendency to them in the affected localities can in any case be increased by anti-hygienic conditions.

The soil can be the cause of an endemic by being the bearer of the cause of disease. Thus is it in many localities with typhoid fever in the fall, and in the various forms of malarial disease, cholera, plague, yellow fever. The latter, at first endemic in a more or less limited district, spread out later beyond their confines into extended epidemics. Cretinism, goitre, are most probably endemic through the nature of the soil; both stand in a relation to endemic intermittent fever.

By means of anti-hygienic regulations, typhoid fever, tuberculosis, scrofula, as well as anæmia, chlorosis, rachitis, have almost become endemic diseases in nearly all great cities.

An abnormal condition of corn is the cause of Pellagra in Upper Italy. Many parasitic diseases become endemic in some localities on account of the abnormal condition of important articles of food, *e.g.* of certain kinds of meat. Contamination of drinking-water causes in many places, chiefly in those not accustomed to its use, endemic intestinal and gastric disorders, probably sometimes also typhoid fever, as well as infection with *Bothryocephalus* and *Ankylostomum*. An abnormal quantity of its normal ingredients, *e.g.* lime, is said to be the cause of many affections in a community.

From more or less unknown causes arise endemically, *e.g.*, in many localities and countries, diphtheritic affections, carcinosis, aneurisms, plica Polonica, and other affections. The formerly unknown causes of many endemics have lately been cleared up, as, *e.g.*, the nature of a form of hæmaturia observed in Africa, through the discovery of a parasite, the *Distomum hæmatobium* (p. 121).

OESTERLEN, *Die Seuchen, ihre Ursachen, Gesetze und Bekämpfung.* 1873.

EPIDEMIC, ENDEMIC, ANNUAL CONSTITUTION OF DISEASE, EPIDEMIC CHARACTER OF DISEASE ; *genius epidemicus:* are expressions for the strikingly frequent appearance of similar diseases of a non-contagious or miasmatic nature, of diseases equally innocent and malignant, and for the striking succession of individual symptoms. Heretofore, with respect to this, nothing serviceable could be brought forward, because of the false views and classifications of diseases (inflammatory, rheumatic, gastric, bilious, nervous, anæmic, scorbutic-putrid, etc.) which were at the foundation of the older observations; in later times, however, these matters have unjustly received no attention.

The following epidemic constitutions have been distinguished :

a. The INFLAMMATORY epidemic prevails preferably during the prevalence of a low temperature, as in winter and during cold north winds, in dry atmosphere. It is characterized by inflammations, for the most part those of the lungs.

b. The NERVOUS epidemic constitution prevails during oppressive heats, scarcity of water, foul atmosphere, as for the most part in the summer, and is characterized by forms of disease which appear with important phenomena connected with the nervous system, and which are asthenic in character, etc.

c. The ANÆMIC epidemic characterizes diseases which make their appearance accompanied by symptoms of anæmia.

d. The GASTRIC epidemic character is developed in those seasons of the year in which heat and moisture prevail together. It disposes to affections of the digestive apparatus ; further, under its influence arise typhous diseases. To the gastric is subordinated the bilious epidemic character of disease, which in very hot seasons of the year disposes to troubles of the hepatic system.

e. The PUTRID epidemic constitution makes its appearance at such times and in those places where, during moderate heat, great quantities of organic substances putrefy, as has been observed after great battles. Diseases thus originating have the septic character.

f. The CATARRHAL epidemic character occasions diseases of the mucous membranes, especially of those of the organs of respiration and of the digestive canal, and prevails at the time of changes of the weather, especially if cold alternate with warmth, as in the spring and autumn. It prevails also in moist cold weather.

g. The RHEUMATIC epidemic constitution, which arises from sudden changes of the temperature during prevailing winds, etc., disposes to those forms of disease which are designated by the one-term rheumatism.

(According to REICH, *Lehrb. d. Allgem. Ætiol.*, p. 287.)

PART THIRD.

GENERAL PATHOLOGICAL ANATOMY AND PHYSIOLOGY.

(Study of local disturbances of the circulation, and of nutrition.)

I. LOCAL DISTURBANCES OF THE CIRCULATION.

WEDEMEYER, *Unters üb. d. Kreislauf des Blutes u. insbes. üb die Bewegung dess. in den Artt. a. Haargeff*, 1828.—WILLIAMS, *Rech. sur les causes du mouv. du sang d. les vaiss. capill.*, 1835.—DUBOIS (d'Amiens) *Préleçons de path. expér.*, 1841.—GRIE-SINGER, *Arch. f. phys. Heilk.*, 1842, I.—BERGMANN, *R. Wagner's Handw. d. Physiol.*, 1844, II., p. 211.—ED. & E. H. WEBER, *Müller's Arch.*, 1874, p. 232. 1851, p. 497.—LUDWIG, *Müller's Arch.*, 1847; *Œstr. Jahrbb.*, 1863, XIX., p. 35.—VOLKMANN, *Die Hämodynamik*, 1850.—BERLIN, *Nederl. Lancet*, 1850.—DON-DERS, *Nederl. Lanc.*, 1850, V., p. 521; *Ztschr. f. rat. Med.*, 1853, III.—STIL-LING, *Jen. Ann.*, 1851, II., p. 179.—VIRCHOW, *Dessen Arch.*, 1851, III., p. 427. V., p. 281; *Handb. d. spec. Path.*, 1854, I., p. 93.—BERNARD, *Compt. rend. de la soc. de Biol.*, 1852, III.; *C. r. de l'acad. d. sc.*, XXXIV. & LV., p. 228, 305 u. 381. ECKER, *de cerebri et med. spin. syst. capill. in statu sano et morb.*, 1853.—LIEBER-MEISTER, *De fluxu collaterali*, GRYPH, 1856.—KUSSMAUL u. TENNER, *Unters. üb. Ursprung u. Wesen der fallsuchtart. Zuckungen bei der Verblutung. sowie der Fall-sucht überh.*, 1857.—BRÜCKE, *Virch. Arch.*, 1857, XII., p. 81.—KÖRNER, *Prag. Vjrsch.*, 1860, III.—AL. SCHMIDT, *Arch. f. Anat. u. Physiol.*, 1861, p. 545; 1862, p. 428 u. 533.—v. RECKLINGHAUSEN, *Die Lymphgefässe u. ihre Bezieh. zum Bindegewebe*, 1862; *Virch Arch.*, XXVI., p. 172.—GOLTZ. *Virch. Arch.*, 1864, XXIX., p. 394. O. WEBER. *Handb. d. allg. u. spec. chir.*, 1864, I., p. 27.—STRICKER, *Wiener Sitzgs-ber.*, 1865, LI., p. 16; LII., p. 379.—EW. HERING, *Wiener Sitzgsber.*, Nov., 1867; LVI., p. 691; LVII., p. 170.—COHNHEIM, *Virch. Arch.*, 1867, XL., p. 1; *Unters. üb. d. embol. Proc.*, 1872—TRAUBE, *Die Sympt. d. Krkh. d. Respir. u. Circul.; App.*, 1867; *Ges. Beitr. z. Path. u. Phys.*, 1871.

(Consult also the later works on Physiology, and the publications of the Physiological Institute at Leipzic, 1866–71.)

[BURROWS, *Disorders of the Cerebral Circulation*, Lond., 1845.—PAGET, *Lectures on Surgical Pathology*, Lond., 1870.—SANDERSON'S *Handbook for the Laboratory*, Phil., 1873.—DALTON'S and FLINT'S *Treatises on Human Physiology.*—VULPIAN, *Leçons sur l'appareil vaso-moteur*, 1874–5.—ED.]

LOCAL DISTURBANCES OF THE CIRCULATION concern the circulation of the blood and that of the lymph. In that which follows notice will be taken of some physiological considerations which have a general pathological interest.

The MOTION OF THE BLOOD is effected chiefly by the heart, its DISTRIBU-TION by the vessels.

The HEART is the most important factor of the blood circulation. The force of the heart's impulse in mammals equals the pressure of a column of mercury 150 mm. high, and yet the physiological limits of this pressure allows of a considerable variation from this mean number. The pressure depend-

ent upon the heart's impulse is variable, and diminishes with the increasing distance from the heart. A further increase of force for the blood is derived from the elastic and muscular elements of the walls of the arteries and veins.

The ARTERIES are always over-filled with blood. They seek, in consequence of their small but very perfect elasticity, to rid themselves of their contents by contraction, and thus by the continuous arrival of new blood from the heart they cause the regular and uninterrupted movement of the fluid through the capillaries into the veins. The smooth muscles found in the walls of the arteries, especially numerous in those of smaller size, are susceptible to mechanical, electrical, thermal, and chemical irritants. The small arteries thereupon contract slowly, strongly, and continuously, the contraction not continuing far upward or downward. A stronger contraction of the arteries is followed by an increase of the resistance of the circulation. In general, in the independent power of the smaller arteries to contract, may be observed a condition for the moderation or regulation of the circulation.

The BLOOD-PRESSURE in an artery increases : 1. With the filling of the vessels generally, as with the quantity of blood, and with the narrowing of the channel. 2. With the frequency and force of the heart's contractions. The mean blood-pressure in the largest arteries in man is not accurately known. In the art. brachialis it amounts to about 115 mm. ; in the aorta it has been estimated at 250 mm. (quicksilver) ; in the smaller arteries it diminishes constantly from the left ventricle to the capillaries. It is less in younger and weakly animals. In the pulmonic it is much less than in the systemic circulation ; in the art. pulmonalis it amounts to 12–30 mm. The pressure of the blood is made to rise by muscular movements, and to sink by long fasting, loss of blood, etc.

Every part of an artery further presents a PERIODICAL FLUCTUATION in pressure : an elevation of pressure corresponding to the heart's systole, and an abatement of pressure corresponding to the heart's diastole—the so-called pulse. This fluctuation in pressure is greatest nearest the heart, least, or almost unnoticeable at the extremities of the arteries. Farther, an elevation takes place during expiration ; a diminution during inspiration.

According to QUINCKE (Berl. klin. Wschr., 1868, No. 34), the arterial wave generated from the left side of the heart does not disappear so generally as has been assumed until now in the small arteries. On the contrary, there are parts in which very often under normal, still more distinctly under pathological conditions, the propagation of the pulse-wave can be observed to continue from the heart into the capillaries, and even through these into the veins : those parts are the finger-nails, the hand, the fore-arm, and the foot. In the nail the capillary pulse can be seen often even under normal conditions, still better in the anæmic, in the elevation of the hand, most distinctly in cases of insufficiency of the aortic valves. Most probably also the brain exerts an active and independent influence on the arterial walls in the motion of the blood through the capillaries. This determines peristaltic, regular contraction of the arteries. (v. BEZOLD, Unters. aus d. phys. Labor. zu Würzb.. 1867, 2. H. p. 347.)

The VEINS are filled in a much less degree than the arteries. The difference in the filling of both kinds of vessels is to be felt through the skin in those which lie near the surface, to be seen in the vessels which have been laid bare, and is to be perceived, especially, from the various heights to which the blood-stream rises when spirting forth from vessels which have been cut. The veins have a layer of circular muscular fibres, which is strongly developed, especially in the lower extremities ; besides, there exists a layer

of longitudinal smooth muscle fibres, especially in the adventitia of the large veins of the abdomen. The action of these muscles effects a shortening of the vessels, their relaxation is followed by the vessels' elongation. In the brain the muscular portion of the veins is extremely little developed, or is entirely wanting. The elasticity of the walls of the veins is much less than that of the arteries; the elastic elements in the veins are also arranged preponderatingly in the direction of the length of the vessels, so that especially the veins of the internal parts of the body are in their diameter unusually dependent on the varying pressure of their contents and of the parts surrounding them.

The BLOOD-PRESSURE in the veins is very fluctuating, and is much less than that in the arteries. In the veins near the heart it amounts to only $\frac{1}{10} - \frac{1}{20}$ of the pressure of the corresponding arteries. It diminishes in the direction toward the right side of the heart. In compression of adjacent veins it increases in those which are free. During inspiration the blood-pressure diminishes in the veins which are near the thorax, and increases during expiration. During inspiration the pressure in the veins is, so to speak, negative, *i.e.*, it is less than that of the atmosphere.

The CAPILLARIES, from one point of view, consist of closely united, flat, nucleated cells, sometimes for the most part spindle-shaped, sometimes polygonal (the so-called vessel-cells, endothelia). Between these cells are to be found openings (stomata) of a perhaps rounded or more or less elliptical outline, in varying number, and in size probably varying greatly with the diameter of the vessel. According to the other view the capillary membrane is not made up of cells, but is a soft protoplasmic tube, and probably permeable to red and colorless blood-corpuscles; it is further, at least in young vessels, formed out of contractile substance, so that it is capable of active contractions. Concerning the adventitia capillaris, so-called, *vide infra.*

HOYER, AEBY, AUERBACH, EBERTH, and many others, support the first view, which is based upon the images formed by the action of silver on dead tissues, while the other view was first advocated by STRICKER, and is based especially upon examinations in living animals. The latter (*Wien. acad. Sitzgsber.*, 1865), and GOLUBEW (*Schultze's Arch.*, V., p. 49), have shown that moderate irritation of the living capillary vessels cause alternating local dilatation and contraction.

The blood pressure in the capillaries has not been measured, but only estimated from their extent and the amount of their filtration. It varies with the general blood-pressure, increasing with the diminution of resistance in the arteries, and with the increase of such resistance in the veins. It changes, also, with the change of resistance of the tissues which surround the capillaries.

The area of a cross-section of the capillaries together amounts to more than 800 times that of the aorta at its origin; that of each vena cava is almost as large as that of the aorta.

According to GOLTZ (*Arch. f. d. ges. Phys.*, 1871, V., p. 53) the EPITHELIUM of the vessels perhaps acts like that of the glands. As the latter, with the co-operation of the nerves, takes up a fluid stream from out of the vicinity of the glands and then moves it into the excretory ducts of the glands, so also may the epithelium of the vessels possess the function of introducing liquid into the interior of the vessels. This character is ascribed chiefly to the capillaries and smallest lymphatics, the walls of which consist only of epithelium. The force with which the liquid moves from the smallest non-muscular vessels into the larger, is then the pressure of secretion, under which the epithelial cells work. The smooth muscles of the vessels behave like those of the excretory ducts of the glands.

In many organs the arteries are probably connected with veins in a two-fold manner: one form is by the capillary circulation, which is characterized as the general, deep, or interstitial, chemical or functional, nutritive circulation ; the other form is effected by a direct communication of arteries and veins without an intermediate capillary system : the so-called mechanical or direct, derivative circulation. The smallest arteries which make up this second form of circulation are about 0.1 mm. thick, and possess organic muscular fibres ; they are so contractile that complete obliteration of the vessels can occur ; they have vaso-motor nerves. These transitions occur besides in the corpora cavernosa of the genitals, the spleen, the placenta, in various parts of the skin, aponeuroses, joints, mucous membranes, muscles, brain, lungs, in part also in glandular organs.

These relations, important in many points of view, with respect to the pathology of the local derangements of the circulation, were already known to LEEUWENHOEK and HALLER. They were accurately described by DUBOIS (1841, l. c., p. 313), PAGET (*Lond. Med. Gaz.*, 1850), and WH. JONES. According to VIRCHOW (*Arch.*, XII., p. 310) a part of the blood in the kidneys can pass directly from the arteries into the veins, while another part of it flows through the Malpighian bodies. BERNARD (*Allg. Wiener med. Ztg.*, 1850, Nr. 40–42) assumes two forms of capillary vessels : those which are comparatively thick and in part retain the course of the original communication ; and those which are exceedingly thin, bathing every cell with liquid, and forming the nutritive network of vessels which belongs to every organ. There are vessels in every organ which restrain the blood, and there are those which permit it to flow on through. Hence it cannot be believed that all the blood which flows through an organ, *e.g.* the kidneys, the liver, contributes to its maintenance ; this is true more often of only a part of it, while another part flows through without suffering any change, and merely effects the mechanical phenomena of the circulation. SUCQUET (*Bull. de l'acad.*, XXVI., p. 825, 1861.—*D'une circul. dérivat. dans les membres et dans la tête chez l'homme*, 1862) found that wide communications existed between arteries and veins in definite localities in the skin of the limbs and head. In the upper extremities, *e.g.*, there exists a double circulation : the deep, nutritive, constant and almost without variety, and the superficial, which is truly derivative ; both forms progress without interruption, but the latter varies with the quantity of circulating fluid, also with the energy and frequency of the heart-beats, as well as also with the action of the vaso-motor nerves, while the former suffers only a slight change. In the head the blood is carried away in like manner through the *vasa arterio-venosa*, out of the arterial into the venous system when the former is over-filled, so that also here the proper capillary circulation can go on independently in a regular and constant manner. Through the communicating cutaneous branches of the ophthalmic artery the blood is carried away from the internal arteries of the cranium into the *venæ frontales et angulares*, while the eye is injected. The communications of the labial, nasal, palpebral and auricular arteries effect a release of the blood in over-filling of the facial, internal maxillary and temporal. Direct communication is accomplished in various ways. Consult also HOYER (*Tagebl. d. Nat. Vers.*, 1872, p. 149). TOMSA (*Arch. f. Dermat. u. Syph.*, 1873, V., p. 1) denies the so-called derivative circulation in the skin : the seats of this lie in those parts of the head and extremities where LANGER has demonstrated a very slight or no tension of the skin (forehead, hand) ; those points where the mass of injection flows with greater velocity, and so has less resistance to overcome, coincide very often with the points of irregular divisibility. Many others likewise regard these assumptions still as undemonstrated.

According to RINDFLEISCH (*Tagebl. d. Nat. Vers.*, 1872, p. 210) vessels of large calibre are formed in pulmonary emphysema, between the extremities of the arteries and the beginning of the veins.

The VELOCITY OF THE BLOOD-STREAM shows constant variations in the several kinds of vessels, which variations are shown partly by means of special apparatuses (hæmodromometer, etc.), in part indirectly by observing the circulation in the living animal (mesentery, etc.). The resistances which influence the velocity of the blood-stream, lie in friction. The

velocity is greatest in the arteries (in the carotid of the dog about 260 mm.,
in the metatarsal, about 56 mm., in a second), less in the veins, least in
the capillaries (in the retina of man about 0.7 mm. ; in the tail of the tad-
pole about 0.6 mm. in a second). In the latter they are moreover subject
probably to manifold essential and accidental variations.

According to DOGIEL (*Arb. aus d. phys. Inst. zu Leipzig*, 1867, p. 196), the velo-
city of the blood in the same arterial branch is subject to great and sudden changes,
in spite of the fact that the heart impulse and the mean blood-pressure remain the
same. DOGIEL demonstrated farther, that the velocity of the streams which exist
in two simultaneously observed arteries, vary altogether independently of each other,
and as independently also of the blood-pressure, so that with the same blood-pres-
sure the velocity in both channels may increase in the same, or opposite directions.

Certain conditions from without have an influence upon the circulation
to assist or to impede it, chiefly by their influence upon the veins. The
course of the venous blood is therefore very irregular.

GRAVITY exerts an irregular influence upon the circulation, sometimes
promoting it, sometimes impeding it ; the former upon descending, the
latter upon ascending veins. In general, pressure acts unfavorably, by
preventing the regular distribution of the blood, and by promoting its accu-
mulation in isolated parts. By this is explained the influence of the sud-
den change from a horizontal to an upright posture, not infrequently giving
rise to fainting in many healthy and strong persons, still more certainly in
the sick and convalescent.

The effect of EXTERNAL PRESSURE upon the circulation is important, since
the vessels, partly in the interior of the body, partly on the surface, and
deep in the extremities, are found continually under such pressure. From
this the arteries suffer little ; the capillaries, and especially the veins, con-
siderably. Every pressure upon a vein is followed by an emptying of the
blood toward the heart, because a turning to one side in an opposite direc-
tion is in most veins prevented by the valves. Such a pressure, if inter-
mittent, as for example, during the muscular movements 'of the extremi-
ties, may be of assistance under certain conditions of the mechanical power
of the heart. But a constant pressure, like that from bands, bandages,
exudations and tumors, affects unfavorably the venous circulation—favor-
ably, however, in the highest degree, when by pressure enlargement of the
vessels becomes reduced. If the pressure itself is elastic, like that from
intestinal gases in the abdomen, it does no harm ; for just as it hinders to
a certain extent the entrance of the blood into the arteries, and through
the capillaries into the *vena portæ*, so it promotes also the stream of the
blood at the time in the *vena portæ* in the direction of the hepatic veins.
The changing pressure from the movements of the diaphragm and from ab-
dominal pressure during respiration aids the abdominal circulation. A
diminution of the pressure from without, as occurs in the climbing of high
mountains, in puncture of ascites, of the eyeball, partially under the cup-
ping-glass, etc., dilates the vessels and favors a retardation of the stream.

COLD causes a contraction, HEAT a dilatation of vessels of every calibre,
even the aorta and the cavæ. Cold causes, first of all, a vigorous contrac-
tion of the muscles of the vessels, which by excess of excitation is second-
arily followed by relaxation. These effects of cold and warmth are inde-
pendent of the vaso-motor nerves.

Experiments of HASTINGS, SCHWANN, O. WEBER.

The larger LYMPHATICS have essentially the same structure as small

veins; an elastic intima provided with endothelium, with numerous valves, a muscular middle coat, and an adventitia.

The LYMPHATIC CAPILLARIES have an endothelial covering, but otherwise no elements of a wall; in general they resemble the blood-capillaries, but the walls are more delicate (on this account visible for the most part only when naturally or artificially injected, or after the cells of which they are formed are colored by silver), more numerous, and much broader. They are arranged with respect to locality, either as networks, which not infrequently accompany the bloodvessels; or, they are blind ducts, which afterward unite to form networks; or, they form sheaths around the blood-capillaries, *i.e.*, they lie between the capillary membrane proper and the so-called adventitia, so that the blood-capillaries are separated from the tissue elements by a lymph-space.

The ORIGIN OF THE LYMPHATICS is not certainly known. It is most probably in the so-called PLASMATIC CANALS—spaces of the smallest size found in connective tissue, without a special membrane, but provided with that unclear so-called endothelium, usually filled only with liquid. In the central nervous-system the beginnings of the lymphatic-vessels are perivascular spaces, *i.e.*, broad canals clothed with endothelium (or perithelium), in the axis of which are found the bloodvessels. In glands the origin of the lymphatic vessels is identical with fissures occurring between the bloodvessels and the glandular canaliculi, etc.

SEROUS MEMBRANES are in open connection with the lymphatics. This takes place by means of small round holes, which in the living, and even after death receive and convey into the lymphatics not only fluids, even such as are not miscible with water, as oil, but also solids, as well those which are changeable in form (milk-globules and blood-corpuscles), as also those (India-ink and cinnabar) which are changeless. Not only liquids pass normally through these openings, but also lymph-corpuscles, which probably have their origin even in the serous membranes. Tendons and fasciæ behave in a similar manner.

The important statements given above concerning the source of the lymphatics generally, and their open connection with serous membranes, which latter MASCAGNI already accepted, we owe to V. RECKLINGHAUSEN, who demonstrated both chiefly by the silver method and by experimentation. Farther important researches concerning these relations are furnished by LUDWIG and his pupils, SCHWEIGGER-SEIDEL, FREY, CHRONSZEWSKY, AFANASSIEW, EBERTH, TOMSA, ZAWARYKIN, HIS, OEDMANSSON, and others. Consult also GOLGI, *Riv. clin.*, 1870, IX., p. 324. Concerning the lymphatic vessels of fasciæ, etc., consult GENERSICH and LUDWIG

The researches of DYBKOWSKY upon the pleura (*Arb. aus d. phys. Anst. zu Leipzig*, 1866, p. 40) are of special practical interest. Concerning the pathological relations of serous membranes, consult LAVDOWSKY, *Arch. f. norm. u. path. Histol.*, V. RUDNEW, and others, 1870, II., p. 74. WINOGRADOW, *Ib.*, 1871, III., p. 1; *Virch. Arch.*, LIV., p. 79. KLEIN and BURDON-SANDERSON, *Med. Ctrbl.*, 1872, No. 2-4.

According to BUHL (*Lungenentz. u. s. w.* 1872, p. 4) the epithelium of the alveoli of the lungs has less the signification of a continued bronchial epithelium than of a lymphatic endothelium spread out on the inner surface of the alveolar wall; bronchial epithelium passes into alveolar endothelium, just as the epithelium of the Fallopian tubes passes into the endothelium of the peritoneum. SIKORSKY (*Med. Ctrbl.*, 1870, No. 52) makes the lymphatic plexus in the walls of the alveoli communicate by means of fine openings with the lumen of the alveoli. Therefore the cavities of the alveoli are wide lymph-spaces filled with air. The considerable quantity of carbonic acid in lymphatic gases (20-40 per cent.: HAMMERSTEN) may for the most part be derived directly from inspired atmospheric air, and its quick transformation into carbonic acid.

According to SCHWALBE (*Med. Ctrbl.*, 1869, No. 30; *Arch. f. mikr. Anat.*, 1870, VI., p. 1), the arachnoidean space of the brain and spinal cord is a lymph-space,

which communicates with the lymphatic-vessels and glands of the neck through the jugular foramen, as well as with the lymph-canals of the three higher organs of sense. (It has no connection with the perivascular spaces of His, nor with the lymphatics of the pia-mater.) In the eye, *e.g.*, there are found two groups of lymphatics; of these the posterior are to us of special interest. To this group belong the perivascular spaces of the retina, the perichoroidal space and its efferent canals, and the lymph-space lying between the internal and external sheaths of the optic nerve, which opens directly into the arachnoidean space of the brain. (The anterior lymph-passages of the eye do not communicate with the posterior. Both chambers of the eye form a system of currents which has its efferent canals at the corneal furrow; the lymphatic vessels of the conjunctiva form a second system, the plexus of small channels of the cornea form a third.)

According to BÖHM (*Würzb. Diss.*, 1868), there takes place, under certain conditions, a resorption of finely suspended fat, or cinnabar, from out of the cavities of the joints, which, therefore, likewise points to an open communication between these cavities and the vascular system. B. (*Virch. Arch.*, 1869, XLVII., p. 218), after treatment of synovial membranes with silver, saw an open connection of the lumina of the bloodvessels with the plasmatic canals.

The flow of lymph out of its vessels into the veins takes place very slowly and under slight pressure. The forces operative here differ from those which chiefly effect the discharge of the lymph : they are aspiration of the thorax and contraction of the muscles surrounding the lymphatics.

HELLER (*Berl. Ctrlbl.*, 1869, No. 35) found in the exposed mesentery of young guinea-pigs a peculiar rhythmical movement, which bears a type independent of all other rhythmical movements of the organism (respiration, pulse).

The cause of the discharge of lymph is the difference between the pressure in the capillaries and that in the lymph-spaces. By ligature of all but one of the lymphatics of the testicle, which are easy of access beneath, and of the spermatic artery, more lymph is discharged in the moderate contraction of the pampiniform plexus than when the venous stream continues unobstructed. Should the arterial pressure be reduced to a minimum, no lymph at all would, as a rule, be discharged. According to LUDWIG, the fasciæ also in a dead animal absorb to their fullest extent liquids which have been injected in such manner as to produce rhythmic tension and relaxation; the colored matter injected is demonstrable in the thoracic duct. During muscular activity in the living, where a like alternation between tension and relaxation of the fasciæ and aponeuroses takes place, those membranes and their lymphatics act like sucking-pumps.

The QUANTITY OF BLOOD in general is considered in Part IV. The quantity in single organs varies greatly under physiological and pathological conditions.

Of the ELEMENTS OF THE BLOOD, the blood-corpuscles, especially the white, and fibrin have a prominent pathological significance.

During the flow of the blood through the capillaries, only the fluid elements pass uninterruptedly out of the latter into the tissues, and out of these, in a modified condition, back again into the vessels; but most probably red and especially white globules normally leave the capillaries to reach the adjacent lymphatics or tissue. This transmigration takes place only where the blood-current is sluggish. It takes place without injury to the vessels, in a manner as yet unknown. The wandering red blood-globules mostly again return into the circulation through the lymphatics. The white globules which have wandered out form, all or the greater part of them, in the various tissues the so-called movable or wandering connective-tissue corpuscles, mucous corpuscles, salivary corpuscles, the corpuscles of the serous cavities, perhaps also the round corpuscles known in the gray and white substance of the central nervous organs. They probably return again into the blood in the same way as the red globules. Consequently the fluid as well as the corpuscular elements of the blood have a double way of re-

turn from the capillaries to the heart: on the one hand, by the veins; on the other, by the lymphatics.

Consult STRICKER, COHNHEIM, HERING (l. c.), HENLE and MERKEL (*Z. f. rat. Med.*, 1868, XXXIV., p. 49).

The cause of the transmigration of the white globules lies, according to COHNHEIM, in their active mobility ; according to SCHKLAREWSKY (*Arch. f. d. ges. Phys.*, 1868, I.), in physical forces. According to HERING (*Wien. Sitzungsber.*, LVI., p. 691, and LVII., p. 170), the homogeneous mass, with which the red globules of the blood dammed up in the vessels appear to be blended, acts, opposite the walls of the vessels, like a liquid colloid substance. If the pressure be sufficiently prolonged, it exudes in isolated drops through the walls of the vessels and slowly extends into the surrounding structures, whereby, if the extravasation extends into a lymph space, the individual blood-globules may again assume their old form.

Direct observations show that the white globules of the blood can probably enter again into the same channel by the same way through which they left it. RECKLINGHAUSEN (*Stricker Hdb.*, p. 249) not only saw the colorless cells pass out of the capillaries, but also migratory corpuscles of the connective tissue enter into them. SAVIOTTI (*Berl. med. Ctrlbl.*, 1870, Nos. 10 and 11) saw the same. He has besides demonstrated experimentally on the web of the frog, that pigment cells send their processes into the vessels through their wall, so that they really migrate as a whole or by pieces into the bloodvessels, and are carried away by the blood-current. This occurs normally, as well as after the employment of means to excite inflammation, in the capillaries as well as in the small, perhaps also large veins.

Under various conditions which always cause a congestive hyperæmia, the number of migrating white globules increases very considerably, and gives rise to suppuration. PUS-CORPUSCLES, so-called, ARE FOR THE GREATER PART MIGRATED WHITE GLOBULES. See INFLAMMATION.

The white globules, which have the properties known in the dead state, show, when alive, a peculiarity, which explains the foregoing facts, and besides is of importance for physiology and pathology ; they are contractile.

THE CONTRACTILITY of the white globules, and of the corpuscles identical with them, is shown in the examination of living animals (foot-web and mesentery of the frog, certain mammals), of freshly dissected animal parts (connective tissue, cornea), of fresh globules in proper menstrua (natural liquid transudations, weak solutions of sugar and common salt, etc.), and when possible, during examination upon the warm stage of fluids containing such bodies (blood, mucus, saliva, pus). The corpuscles do not then appear round, but present points of various lengths, numbers and forms. Each corpuscle changes its form continually, sending out quickly fine filamentous processes, singly or in groups, which processes thicken at their base and consist of a part of the substance of the cell-body. They again retract and disappear without leaving any traces of their existence behind. Sometimes these processes appear on the whole circumference of the pus-corpuscle, from ten to twenty in number, sometimes tufts of from three to six appear in one or more points of the periphery. The single shoots of the corpuscles may branch again and unite with one another in twisted forms, and then flow together into one broad mass. The corpuscles contain nuclei, which become visible only by means of reagents. They also contain molecular fat and pigment, which change their locality in the cells with their motion (so-called MOLECULAR MOTIONS), these motions being most marked where processes are given out from the cells.

The corpuscles exhibit these changes of form as well in liquid connective substances (humor aqueus, serous membranes) as in solid tissues (cornea, connective tissues chiefly), and consequently they wander in them, for the

most part in very circuitous routes. Migration is accomplished in the following manner: the cell-mass shoots out into processes, then the round end opposite to the process advances with it in line, and then, by a farther elongation of the body of the cell, it moves on still farther. This migration takes place, as already said, not merely through open spaces or cavities of the connective tissue, but also through the walls of the capillaries and small veins.

Contractility of animal cells was observed in the white globules of higher and lower animals, by WM. JONES, DAVAINE, ROBIN, ECKER, LIEBERKÜHN, HAECKEL; in lymph-corpuscles, corpuscles of the spleen, mucous corpuscles, in similar cells in the transudation of serous membranes, etc., by BUSK and HUXLEY, LIEBERKÜHN, VIRCHOW, RECKLINGHAUSEN, OEHL, COHNHEIM, etc.; in the segmented globules of the frog's ovum, by STRICKER; in pigment cells, by BRÜCKE, VIRCHOW, LOTH. MEYER, WITTICH, BUSCH; in pigment-cells of colloid tissue of lower animals, by HUXLEY and KÖLLIKER; in the cells of enchondroma, by VIRCHOW; in giant cells, by LANGHAUS, etc. But RECKLINGHAUSEN first demonstrated the regular occurrence and pathological significance of that peculiarity, especially in pus-corpuscles.

LIEBERKÜHN (*Ueber Bewegungserscheinungen der Zellen*, 1870) holds especially that molecular movements within the body of the cell, the formation of vacuoles in the same place, as well as certain phenomena of elasticity, which have been regarded as phenomena of contraction, and the true movements of the body of the cell, are independent of one another. The proper contractile movements of cells, whereby they change their external form, are independent of the movements of contractile substances, which relate to the appearance and disappearance of the vacuoles.

ROTH (*Virch. Arch.*, XXXVI., p. 145) makes prominent the great harmony which prevails with respect to the chemical reaction of fluids or tissues in which the phenomena of protoplasmic motion are observed. This reaction is almost universally feebly alkaline, seldom neutral, never acid. This chemical condition is probably necessary to hold in solution the albumen (KÜHNE'S myosin), which is the basis of the phenomena of life.

From observations directly made by SCHULTZE (*Arch. f. micr. Anat.*, I., p. 1) and others, an elevation of temperature was found to accelerate the protoplasmic movements of white blood-corpuscles and make them more active. According to SCHENK (*Wien. acad. Sitzungsber*, 1869, LX., p. 25) the blood-corpuscles of cold-blooded animals still move at − 5°, those of warm-blooded animals at − 3° C. The blood-corpuscles of batrachians may be frozen for hours at a time, and still move when warmed to 40° C.; in those of rabbits this was the case only when they had been frozen for 10–15 minutes. Sometimes the white corpuscles of man, without special preparation, exhibit movements 10, 20 hours and longer after death.

According to BINZ (*Arch. f. micr. Anat.*, III., p. 386) quinia acts very deleteriously on the movements of protoplasm, especially of the white globules.

According to SCHARRENBROICH (*Med. Centr.*, 1867, Nr. 52) the migration of white blood-globules into the mesentery of the frog becomes very insignificant, if a solution of quinia (certainly in great, unusual doses in therapeusis) be painted on, or injected under the skin.

By the employment of the moist chamber and warm object-plate, amœboid movements and processes of division in red globules were first observed by PREYER (*Virch. Arch.* 1864, XXX., p. 426), then by ROLLET, KLEBS, BEALE, and BASTIAN; FRIEDREICH (*Ib.*, XLI., p. 395) observed them in bloody urine without these helps (probably in consequence of the ingredients of the urine). FR. observed the same also in two cases of leucocythæmia; HELLER (*Unters.*, p. 26) likewise, and in a case of pneumonia; MOSLER in leucocythæmia. Many other observers, however, deny the contractility of the red-corpuscles.

COLORLESS CORPUSCLES, by their contractility, are also able to TAKE UP and TRANSPORT FOREIGN SUBSTANCES (carmine, cinnabar, milk-globules, red blood-corpuscles, dust of every kind, etc.).

Injection of coloring matters, especially cinnabar, into the veins, followed at varying intervals after by examination of the tissues and organs of the body, promises manifold results bearing on physiological and pathological conditions. A very small portion of the coloring matter probably passes out of the

capillaries free or extra-cellular, but the greatest part of it, after being taken up by the white blood-corpuscles, passes out intra-cellular. The passage, physiologically important, of white blood-corpuscles into the secretions, *e.g.* saliva, mucus, milk, has not yet been demonstrated. Injection of coloring matters have been performed by pathologists especially to learn the fate of white blood-corpuscles filled with granules of coloring matter, and which have wandered out of the vessels. Many believe the conclusion authorized, that every young tissue-element (epithelial cell, cylindrical cell, muscle cell, etc.) which contains such molecules after injection of coloring matter, is a white blood-corpuscle in the process of metamorphosis into an epithelial cell, etc. This is not justified, since molecules may penetrate into very soft young tissue-elements after they have become intra-cellular, or if they were until then extra-cellular.

The various tissues and tissue-elements harbor the coloring matter in various ways; sometimes in great quantity, sometimes in very small quantity, and sometimes not at all. Experimentation concerning these matters show in many points no important differences.

That the white globules absorb foreign substances into their interior was first made known by HAECKEL, then by COHNHEIM, RECKLINGHAUSEN, etc. ; the same, with respect to the red globules, was demonstrated by PREYER and LIEBERKÜHN.

PONFICK (*Virch. Arch.*, 1869, XLVIII., p. 1), also HOFFMAN and LANGERHAUS (*Ib.*, XLVIII., 393), found the following with respect to the continuance of coloring matter (mostly cinnabar, seldom aniline blue and ultramarine) after its introduction into the veins of frogs, rabbits, guinea-pigs, and dogs. After a few hours (4–6) the coloring matter was almost altogether taken up by the white globules. Somewhat less quickly (to 24 hours) a small quantity of it disappeared from the circulation ; whereas a great quantity remained in it after many weeks. Cinnabar, inclosed in large cells partly occupied by blood-globules, was found in the blood of the splenic veins after 148 days. The spleen, liver, and marrow of bones contained cinnabar in the intravascular tissues at nearly the same time and in equal degrees.

The spleen and bone-marrow each time included cinnabar in the elements of their peculiar tissue. The latter showed it within its various forms of cells, with the exception of the giant-cells and small round cells. No coloring matter was to be found in the Malpighian bodies of the spleen, nor in the supporting connective-tissue network of the spleen and lymphatic glands. In the liver, cinnabar was the frequent cause of capillary embolisms. Its accumulation in the capillaries follows very quickly, and it is contained within the white globules of the blood. For from 4 to 6 days it is quite uniformly distributed in the acini ; later, in guinea-pigs, its accumulation predominates in their central ; in rabbits, in their peripheric half. The hepatic cells never contain them. According to PONFICK, cells containing cinnabar are found only outside of the vessels in the lymph-spaces in the neighborhood of the capillaries. Coloring matter is always found for a certain length of time in the vessels of most organs, and then at the earliest moment after the twenty-first day they again become extravascular in the tissue, and indeed, as it seems, always in the fine connective-tissue corpuscles ; as in the cornea, conjunctiva, iris, cicatrices, subcutaneous tissues. The spread of granules of cinnabar in the individual organs is very inconstant. They are often found in the tongue (especially its mucous membrane), in the salivary glands and pancreas ; in the mucous coat, seldom the submucous, of the intestinal tract, almost never in its muscular and serous coats. On the twenty-first day the kidneys contain cinnabar, not infrequently distributed over the whole organ with great uniformity, in the corpuscles of the interstitial tissue. They are likewise to be found in the connective-tissue corpuscles of the supra-renal glands and testicles. (In an impregnated animal neither the embryo nor placenta contained cinnabar.) It was more often found in the mucous membrane of the larynx and trachea. The lungs were always very rich in it, on account of numerous capillary emboli. Bone and cartilage-corpuscles never contained cinnabar ; it was more often found in the synovial membranes, Haversian canals and intermuscular tissue. The brain and spinal cord even were very destitute of it. The lymphatic glands of the wound of operation, of the mesentery, and of the liver contain cinnabar very soon after the injection ; partly free in the lymph-sinus, partly in the round cells, or in the latter

only, never in the reticulum. Cinnabar was found only very late in the remaining lymphatic glands, and indeed only in the lymph-sinus and ducts. Cinnabar has never been demonstrated in cartilage, bone, and epithelium, only in small quantity in the central nervous system.

REITZ (*Wien. acad. Sitzgsber.,* 1858, LVII., p. 8) saw granules of coloring matter, after injections of cinnabar into the blood, in those elements also, which had never been contained within the vessels : as in the epithelial cells of all the mucous membranes ; likewise in the cartilages, in the cells as well as in the intercellular substance (also HUTOB and HEITZMANN). The quantity of coloring matter was so much greater, if inflammation affected the localities in question. In an impregnated rabbit, coloring matter was found not only in the uterus and placenta, but also in the blood of the fœtus, especially abundant in the capillaries of the pia-mater. The presence of cells containing coloring matter in a mass of inflammatory origin does not yet decide these cells to be migrated white blood-cells without further investigation.

Colored particles, especially of coal-dust, are very commonly found within the mucous corpuscles of the upper part of the respiratory tube. How this and other dust penetrates into the deeper air-passages, lungs, etc., is not yet accurately known.

White blood-globules as well as wandering cells sometimes also take up red and white blood-globules and even epithelial cells, and move away with them. The former takes place sometimes in the same manner as with coloring matters, and the red globules thereby are usually divided into many smaller parts ; but sometimes the wandering cell surrounds a much larger cell, altogether or by leaving a part free. (HOFFMAN, *Virch. Arch.,* LI., p. 373.)

The CAUSES OF SECRETION OF FIBRIN OR OF ITS FORMATION are of importance, with respect to the theories of thrombosis, dropsy, and inflammation.

Fibrin is formed by chemical combination of a FIBRINOPLASTIC substance belonging to the contents of cells, with a FIBRINOGENIC substance peculiar to the intercellular fluids. The fibrinoplastic substance (paraglobulin) may be discharged in a solid form from the fluids containing it, not however in a pure state, but mixed with other bodies. Red corpuscles especially are fibrinoplastic. Chyle, lymph, pus, corneal tissue, the umbilical vessels, the lens, indeed almost all cellular elements, are fibrinoplastic; finally, fluids in which the cell-contents are transformed, as blood-serum, the humors of the eye, saliva, synovia. The white of the egg, tendon and cartilage are not fibrinoplastic. Fibrinogens are not only those coagulating spontaneously, but almost all serous fluids, which by the addition of a fibrinoplastic substance are coagulated. The white of the egg, the humors of the eye, normal synovia, have no fibrinogenetic property. Fibrin is secreted under normal conditions, if the fluids, *e.g.* the blood-plasma, which contain both generators of fibrin, have been withdrawn from the living body. In the body even, coagulation of the blood is prevented, through the influence of the walls of vessels.

BRÜCKE has demonstrated by numerous experiments, that the wall of the vessels and indeed the inner membrane of the bloodvessels, as well as of the lymphatics, and serous membranes, prevent coagulation of the blood in living vessels. He exposed blood at a temperature of almost 0 C. for fifteen minutes to atmospheric air, then returned it into the heart or vessels of an animal just dead and hung it up in a room saturated with moisture. The blood remained liquid many hours in warm-blooded, many days in cold-blooded, animals. During this time a drop of blood drawn from the vessels coagulated immediately. If a foreign body was introduced into the vessel, the blood coagulated only in its vicinity.

We are indebted to AL. SCHMIDT for the demonstration of the fact, that fibrin has its origin in the combination of fibrinoplastic with fibrogenetic matter.

That blood-cells are the bearers of fibrinoplastic material is known from this, that coagulation first begins in their vicinity and spreads hence into the remaining liquid. Also, from the fact, that blood-cells in giving rise to coagulation act differently,

after interference with their nutrition, *e.g.* in not being able to take up sufficient oxygen. Hence, it must be admitted that they cannot develop fibrinoplastic substance in a normal manner, in inflammatory affections, to wit, of the thoracic organs, and in apnœa; the effect must be greater in the simultaneous increase of fibrogenetic substance. Slow coagulation of the blood in such cases is nevertheless known.

In general, the slower the coagulation, the softer, more gelatinous and more incapable of contraction is the coagulum, and so much the less fibrinoplastic substance there was in the liquid.

With respect to the influence of gases on the coagulation of the blood:—the presence of carbonic acid retards coagulation. In this manner also other weak acids act, as well as alkalies and alkaline salts. Oxygen and atmospheric air have no direct influence on coagulation, for blood kept a whole week in the air retains its efficiency. Coagulation is retarded not from the want of oxygen but by the accumulation of carbonic acid, as well as by the simultaneous deterioration of fibrinoplastic activity. Transudates remain fluid longer in closed cavities of the body than in the air, because the carbonic acid contained in them cannot escape.

Coagulation is promoted by contact with the air, with foreign solid bodies, by a temperature elevated to 55° C.

Blood which had been taken from animals half an hour after death, always coagulated much more slowly than that drawn earlier. This gradual loss of energy in spontaneous coagulation is the rule in blood from the dead, especially in that of those who had died from suffocation.

According to AL. SCHMIDT (Dorpat, 1872), a FERMENT arises in the blood withdrawn from the vessel-walls, under the influence of the blood-corpuscles, which ferment induces coagulation of fibrin. The fibrinogenic and fibrinoplastic substances furnish the material for fermentation, which substances together must be exposed to the influence of the ferment, to induce fibrin-coagulation. The action of the blood-corpuscles on fermentation depends upon hæmoglobin. Most transudates taken from the cavities of dead bodies contain both generators of fibrin, and no ferment. They coagulate on the addition of the ferment. Others, in which fibrinoplastic substance is wanting, require its supply for the production of coagulation. Neutral alkaline salts interrupt, low temperature wholly prevents coagulation.

According to MANTEGAZZA (*Ann. univ. di medic.*, CCXVI., Apr. 1871, Milan), coagulation of the blood and of other coagulable liquids depends upon a state of irritation of the white-corpuscles, which, in contact with foreign bodies or inflamed tissues, or especially, if they are removed from their physiological conditions, secrete a substance, which is itself fibrin, or the cause of the formation of fibrin.

According to BOLL (*Arch. f. Anat. u. Phys.*, 1870, p. 718) the blood and serous fluids of the embryo are incapable of spontaneous coagulation.

The fluidity of the blood is dependent upon a normal state of the eudothelium; and affections of the endothelium, in which the cells need not as yet have lost their vitality, are causes of coagulation. (See INFLAMMATION.)

The QUANTITY OF LYMPH is not known with respect to the whole body, nor with respect to single organs and tissues. Many estimate it at from a fourth to a third and more of the whole weight of the body. It naturally varies with the general and local quantity of the blood, with the activity or rest of the organ, etc. Not equally striking are the different relations of the quantity of lymph under pathological conditions. (See DROPSY.)

GENERSICH (*Arb. aus. d. phys. Anst. zu Leipzig*, 1871, V., p. 53) found not only that during artificial circulation in the surviving muscles of the extremities true lymph is still produced, but that also there were great differences in its quantity, dependent upon rest and motion. During muscular action from electric irritation the quantity of lymph obtained from tendons and fasciæ, in many trials and with artificial circulation, was more than three times as great as that obtained during rest. A considerably greater quantity of lymph was collected during passive motion than during contractions induced by the galvanic current. The pressure on the lymphatic vessels induced by muscular movements, is, probably, not as important a cause of acceleration of the lymph-stream as the tension and relaxation of tendons and aponeuroses connected with active and passive motion. Still more striking is the

difference between the quantity of lymph excreted during rest and motion without the employment of artificial bloodletting.

LESSER (*Arb. aus. d. phys. Anst. zu Leipzig*, 1872, VI., p. 94) very often observed considerable quantities of lymph flow in a very continuous stream from the thoracic duct of dogs, whose extremities had been completely paralyzed by curare, and whose stomachs and small intestines were free from food. In a dog after fasting, *e.g.*,

Weighing 23860 grm., with 1835 grm. (hypothetical) of blood, 315 C. cent. in 4 hours.

"	24750	"	"	1904	"	"	"	"	296	"	"	6	"
"	15290	"	"	1169	"	"	"	"	261	"	"	$5\frac{1}{6}$	"
"	18600	"	"	1431	"	"	"	"	327	"	"	$7\frac{1}{2}$	"

The mean flow per minute was between 0 and 1.24 C. cent., most frequently 0.3 to 0.8 C. cent. The peculiarity also of the animal probably played a great part. In two cases, lymph flowed for 69 minutes after death at the heart, with almost the same rapidity with which it had flowed a short time before. This, according to the author, is the result of the varying pressure which artificial respiration exercises on the abdomen, and which, in other cases, is caused by the artificial extension and flexion of the limbs. When the posterior extremities were simultaneously flexed and extended, the lymph-current, as GENERSICH had already discovered, was each time considerably swifter than during rest; in many experiments, in the proportion of 5.7, or 4.6, or 2.5 : 1. Lymph which flowed during a state of rest was in most cases opalescent (from fatty floculi); that, on the other hand, obtained during motion, was entirely clear or slightly milky. The latter, transparent lymph, proceeded probably from the posterior extremities, the former from the abdominal viscera. The large secretion of lymph, which appears during poisoning by curare, is connected with lowering of the blood-pressure, so often observed during the action of this poison on dogs. The accelerated lymph-current and lowering of the blood-pressure depend upon a congestion of the abdominal viscera.

THE CIRCULATION WITHIN THE CAVITIES OF THE BODY deserves an especial consideration.

In the THORACIC CAVITY inspiration greatly promotes the streaming of venous blood from all the vessels of the body into the heart; usual expiration exerts no essential influence, while laborious expiration acts as a hindrance. Besides this aspiration of the blood, especially from the vessels of the neck and head, disturbances in the lesser circulation are in inspiration relieved: the lungs develop at this time, and the resistances in the more obstructed vessels decrease. If expiration be long prolonged, as, *e.g.*, in impaired elasticity of the lungs in vesicular emphysema, hindrances to the entrance of venous blood into the thorax increase, the veins of the neck swell, etc. In proportion as the elasticity of the lung tissue fails, the pressure of the air in the lungs increases and renders more difficult the circulation of the blood through them. In the arteries during inspiration there is a lowering, during expiration an elevation, of the blood-pressure.

The conditions in inspiration are important as regards injuries of the large veins near the thorax, since the central end of such a vein sucks in air during inspiration, causing the greatest disturbances of the circulation, and even instantaneous death.

By passing a stream of blood through lungs which had been removed from the thorax, it was observed that the stream passed slowly into the organ in a collapsed state, quickly into it when moderately distended with air, and when the lungs were fully distended the stream at first passed quickly, but soon became slow. (LUDWIG.)

In the CRANIAL CAVITY the blood-capacity likewise varies. In children, when the bones of the cranial vault are movable and the fontanelles open, rising of the brain during expiration and its sinking in during inspiration can be seen and felt; a pulsation even of the brain-mass can there be observed in some cases, just as in adults after injury of the cranium with loss of substance. But the cranium being closed, the explanation of a deficient or

full supply of blood to its contents is more difficult. In dead bodies of
adults and children, one can become convinced of the most various degrees
which exist with reference to the blood-supply of the brain. And too
great effusions of blood, exudations, tumors, etc., could not arise in the
brain, unless room for them could be found within the cranial cavity.
Finally, the increase and diminution of the filling of the vessels have been
directly proven by microscopic examination of the pia-mater of living ani-
mals through a piece of glass hermetically fastened in an opening in the
skull, made by a trephine.

In general, the cranium of adults is a closed immovable capsule, filled
by the brain with its membranes, the cerebro-spinal fluid, and the vessels.
The brain is quite incompressible. If we admit brain-pressure because we
see the brain dislodged by depressed bone, blood-effusions, exudations and
tumors, there is question in chronic cases, of atrophy of the brain, in
acute cases, only of displacement of movable matter. The latter can be
only the blood or cerebro-spinal fluid. Either of these must be displaced into
the spinal canal, which is capable of slight expansion through the elasticity of
the intervertebral ligaments and by the possibility of a sudden depletion of the
blood of the veins of the spinal cord through the intervertebral foramina.
In the brain, it does not happen as in the spinal cord, that there is a con-
tinuous sub-arachnoidal space, but here are found many larger and smaller,
only partly connected spaces. The larger of these, between the cerebellum
and medulla oblongata and under the pons, cerebral crura, fossæ Sylvii,
etc., connect directly with the sub-arachnoideal space of the spinal cord, while
the smaller connect in part with one another in the corresponding sulci, but
not with the larger spaces. Either the arachnoideal fluid flows through the
lymphatic vessels into the neck, or through the communications with the
lymph-channels of the three higher organs of sense into these. This view
of the relation mentioned between the blood and the cerebro-spinal fluid is
also supported by the fact, that in dissection the quantity of the blood of the
brain is found to be in inverse ratio to that of the cerebro-spinal fluid. But
it must always be admitted, that the beginning of changes in the quantity
of blood in the cranial cavity, is rendered difficult in comparison with other
organs.

DONDERS, in the above-mentioned experiments, showed that by increasing the
pressure of expiration, a vessel of 0.04 mm. diameter enlarged to 0 14 mm., and one
of 0.07 mm. to 0.16 mm. ; and that in the sudden deprivation of blood, the vessels
contracted from 0.46 to 0.38, from 0.41 to 0.29, from 0.18 to 0.14 mm.
The cerebro-spinal fluid, the spiral course of the four great arteries of the brain
before their entrance into the cranial cavity, their connection with one another and
arrangement, so that all the vessels are lost in their branches in the pia-mater out-
side of the brain—all these result in this, that within the substance of the brain and
spinal cord arterial blood flows under proportionately slight pressure, and that it also
shows only in a very moderate manner the periodic changes of pressure of the pulse.
To this apparatus belongs, perhaps, the perivascular lymphatic spaces, which commu-
nicate freely with the peri-cerebral spaces, and through these with the lymphatic
vessels of the pia-mater (His, Ztschr. f. wiss. Zool., XV., p. 127). According to BÖHM
(Virch. Arch., XLVII., p. 218), the veins of the outer surface of the dura are some-
how in open communication with the serous cavity of the brain. Probably this is
effected by means of a network of lymphatic vessels, which open on the inner surface
of the dura, but on the other side is in direct communication with the veins.
In the brain the arachnoid is separated from the dura by a capillary layer of liquid ;
in the spinal canal the serous cavity is reduced to null; the arachnoid lies immediately
upon the dura. QUINCKE (Arch. f. Anat., Phys., etc., 1872, p. 153) injected an emul-
sion of cinnabar into various parts of living animals, into the sub arachnoid space of
the spinal cord, into the arachnoid and sub-arachnoid spaces of the brain. A commu-
nication was thus first shown to exist between the sub-arachnoid spaces of the brain

and spinal cord. A current is found in the sub-arachnoid fluid during life, from behind forward, as well as in the opposite direction. This is respiratory in character (MAGENDIE): the yielding venous plexuses of the spinal canal sink in during inspiration, and swell out during expiration more strongly than the fixed cranial sinuses (ECKER, *Physiol. Unters. üb. d. Bewegungen des Gehirnes u. Rück nmark*, 1843). The cerebro-spinal fluid is thereby, during expiration, driven out of the spinal canal towards the cranium, while inspiration is followed by an opposite effect. There exist openings of communication in the arachnoid between the arachnoid and sub-arachnoid spaces of the brain and spinal-cord. The channels for the escape of the cerebro-spinal fluid are numerous. A part leaves the cerebro-spinal cavities together with the nerves; along with these channels appear to exist, which usually convey only liquid. Besides, the current passes the cervical lymph-glands, in the dog the upper-posterior and the maxillary glands. Further, fluid passes out of the arachnoid and sub-arachnoid spaces through the Pacchionian granulations (A. KEY and RETZIUS). Finally, the sub-arachnoid fluid is regarded as passing constantly and normally into the sheath of the optic nerves; the latter is a projection with yielding walls of the sub-arachnoid space. Coloring matter is always found most constantly and in very great quantity in the sub-vaginal space (*i.e.*, in the space between the external and internal sheath of the optic nerve). Whether the supra-vaginal lymph-space also (*i.e.*, the space between the external optic-sheath and the *musc. retractor bulbi*) communicates anteriorly with Tenon's space, posteriorly with the arachnoid space, is in question. The fluid of the sub-arachnoid spaces of the brain and spinal cord rarely reaches the connective-tissue stroma of the choroid plexus, never the ventricles of the brain. On the other hand, a continual current appears to exist from out of the fourth ventricle into the sub-arachnoid space. Magendie's foramen, so-called, probably does not exist. The ways of communication lie in the intermediate spaces of the connective-tissue meshes which form the pia. (QUINCKE.)

Consult ALTMANN, *Der Kreislauf in der Schädelrückgratshöhle*, 1871.

According to LIEBERMEISTER (*Prag. Vjrschr.*, 1864, III., p. 31) the real function of the thyroid gland is to regulate the supply of blood to the brain; the aggregate area of a cross-section of its four arteries is not much less than that of the arteries which provide for the brain; as to the brain, blood is also sent to it from each of the four large arteries destined to the upper half of the body. According to MAIGNIEN and GUYON, the thyroid gland swells during strong blood-pressure and compresses the carotids, thereby preventing a too great blood-pressure in the brain.

In the ABDOMEN, especially in the vena portæ, the conditions of the circulation are in general important, because of the great quantity of blood within its vessels, and in particular because of the theory of hæmorrhoids, abdominal congestions, abdominal plethora, etc. The absence of valves in the portal vein renders it certainly possible for the blood, hindered in its onward flow, to return easily and quickly into the roots of the vein (the hæmorrhoidal veins, etc.). By this also is the circulation equalized, and a hæmorrhoidal bleeding can the more quickly diminish the pressure on the whole system. In a similar manner is explained the swelling of the spleen during digestion: the blood is crowded into the splenic veins, because at this time the gastric and intestinal branches of the portal vein are more largely supplied. The slower circulation in the portal vein, due to its distance from the heart, and to the passage of the blood through a second system of capillaries in the liver, is assisted by the respiratory movements, by the pressure of intestinal gases, and by the pressure of the abdominal muscles.

G. E. STAHL, by his work: *De vena portæ, porta malorum hypochondriaco-splenetico-suffocativo-hysterico-hæmorrhoidariorum*, Hal., 1698, laid the foundation for the study of the maladies connected with the portal vein. According to him, the blood within the territory of the valveless portal vein may easily be displaced by a kind of peristaltic movement of its walls, and accumulate, sometimes in the stomach, sometimes in the spleen, sometimes in the intestines.

According to LUDWIG the stream in the hepatic veins is considerably retarded as soon as the atmospheric pressure upon the liver is only a little increased by means of a force-pump.

Concerning the DEPENDENCE OF THE CIRCULATION UPON THE NERVES, the following points are worthy of attention.

The cardiac nerves arise—not including the intra-cardial nerve-centres—from the cervical portion of the sympathetic, and from the vagus (from its trunk as well as from the recurrent nerve): both nerves together form the cardiac plexus. The vagus is the nerve of arrest, the sympathetic the excitor nerve of the heart's motion. Section of the vagi in the neck causes an increase in the number of the heart's contractions, two-fold and more; moderate excitation (mechanical, chemical, or electrical) of the same nerves diminishes the number of contractions, while strong excitation is followed by complete cessation of the heart's movement in diastole. Irritation of the medulla oblongata, as well as of the upper part of the cervical portion of the spinal cord, acts in the same manner as irritation of the vagi. The effects of irritation or section of the sympathetic are less certain: the former causes, for the most part, an acceleration; the latter, a continuous lowering of the heart's contractions.

The constant excitation of the vagi in warm-blooded animals is REFLEX in character (BERNSTEIN). Of the other reflex irritations of the vagus, are known: mechanical irritation of the intestines in the frog (GOLTZ), perhaps also in many cases in man; irritation of most various sensory nerves (LOVÉN), but only so long as the cerebrum is preserved (CYON); also irritation of the trigeminus by chloroform, ammonia, etc. (KRATSCHMER—HERING, *Wien. acad. Ber.*, 1870, LXII.); that of the abdominal and cervical cord of the sympathetic (BERNSTEIN), of the vagus of the other side (BEZOLD, ETC.). Moderate expansion of the lungs increases the heart's beats; not in consequence of increased pressure, etc., upon the external surface of the heart, but in a reflex manner through the vagi. The sensory nerve-fibres of the lungs, irritated by this expansion, act on the cerebral centre of the inhibitory nerves of the heart in a similar manner as act the fibres of the depressor nerve on the cerebral centre of the vaso-motor nerves: both centres are in a state of continual excitation, which is reduced by irritation of the nerve-fibres mentioned. These fibres are thus the nerves of inhibition for those centres (HERING).

Digitalis excites the inhibitory nerves of the heart, and the peripheric extremities of the vagus, since the action also appears after section of the vagi; thus it reduces the frequency of the pulse. Atropine paralyzes the nerves of inhibition, and thus the pulse is increased in frequency. If atropine first and then digitalis be injected into an animal, no decrease of the frequency of the pulse will be observed (Researches of TRAUBE, BEZOLD, ACKERMANN). DOGIEL saw the heart come to a standstill at the beginning of chloroform inhalation.

A branch of the vagus discovered by LUDWIG and CYON, mostly from the superior laryngeal, the *nervus depressor* (which passes from the heart to the nervous centre of the vessels in the spinal cord), probably diminishes the resistance opposing the emptying of the blood of the over-filled heart. Irritation of its central end is followed by dilatation of the vessels and diminution of blood-pressure. Irritation of its peripheric end, as well as section, is without effect.

The DEPENDENCE OF THE VESSELS UPON THE NERVES consists in this, that the latter keep the muscular fibres of the arteries in constant tonic contraction, so that an active resistance is opposed to the expansion of the vessels from blood-pressure. This continuous excitation upon the arterial wall is exercised by the sympathetic. After section of this nerve in the neck the lateral pressure of the walls of the vessels instantly diminishes; the blood, in proportion to its pressure, dilates the arteries, and, farther on, the capillaries of the corresponding side of the head, and runs through them with such velocity, that, since nutrition does not increase with the quantity of blood, it does not become venous, but remains arterial, and that besides, since the resistance of the arteries is destroyed, the pulse continues into the capillaries, and even into the veins: in consequence there occur reddening and an elevation of temperature from 3°–6° C. On

the other hand, irritation of the superior cervical ganglion is followed, but more slowly, by contraction of the same vessels, paleness and lowering of the temperature. These influences of the nerves occur physiologically in blushing and in paleness. (Both forces have no influence upon the calibre of the veins.) The differences in the temperature of the sick and healthy sides again recede to the normal condition in the animal under experiment, but becomes prominent again during active movements. The differences are especially striking in coldness, loss of blood, pain, in short in all those states which mark weakness in the animal.

Investigations by DUPUY (1816), especially however by BERNARD (1849 and 1852), also by BUDGE, WALLER, BROWN-SÉQUARD, SCHIFF, v. d. BECKE-CALLENFELS, DONDERS, and others.*

The general CENTRAL ORGAN FOR THE NERVES OF THE VESSELS is in the medulla oblongata : irritation of it in the uninjured spinal cord and sympathetic is followed by contraction of all the smaller arteries (with consecutive high raising of the blood-pressure in the arterial branches). This constant irritation is probably due to the influence of the carbonic acid of the blood. In suffocation, the same strong contraction of the smaller arteries takes place from a similar cause. This tonicity of the vessels is destroyed by section of the spinal cord in the cervical region : all the muscles of the vessels of the body relax, with considerable fall of blood-pressure.

According to BUDGE (*Med. Ctrbl.*, 1864, No. 25), the centre of the vaso-motor nerves lies in the cerebral peduncles ; according to others, still higher, in the cerebrum : the latter may at least exercise an influence on that centre.

OWSJANNIKOW (*Arb. aus. d. phys. Anst. zu Leipzig*, 1872, VI., p. 21) has experimentally circumscribed the localities from which the vaso-motor nerves receive their tonus, and in which they receive their reflex excitation. In rabbits and cats the upper limit of this locality is 1–2 mm. below the corpora quadrigemina, the lower 4–5 mm. above the calamus scriptorius.

According to GOLTZ (*Virch. Arch.*, XXIX., p. 394), besides the medulla oblongata, the spinal cord also is throughout an independent central organ for the vaso-motor nerves. This has recently been confirmed by HEUBEL (*Virch. Arch.*, 1872, LVI., p. 248). According to his experiments on the frog, destruction of the medulla oblongata and spinal cord causes the circulation of the blood and resorption to cease, whilst by removal of these organs the continual state of excitation of the whole system of vaso-motor nerves is destroyed, the smooth-muscles of all the vessels are relaxed, the *tonus* of the vessels, and with it the tension of the blood in the vessels, indispensably necessary to the circulation, disappears.

According to M. HAFIZ (*Arb. aus. d. Leipz. phys. Inst.*, 1870, p. 95) contraction of the arteries of muscles does not so uniformly follow irritation of the spinal cord, as is the case with other arteries ; it is always absent in poisoning by curare, while other arteries are contracted. The vaso-motor nerves of muscles are more easily exhausted than others, so that contraction appearing during irritation of the spinal cord very soon passes into dilatation. It follows, then, that not all arteries are materially contracted during irritation of the spinal cord. This is certainly true, however, of the vessels of the skin and intestines.

According to S. MAYER (*Oestr. med. Jb.*, 1872, p. 111) strychnia causes a colossal increase of pressure in the arterial system, which depends upon an extraordinarily intense irritation of the vaso-motor centre in the brain, and the resulting contraction of the small arteries. Nicotina (SURMINSKY, *Z. f. rat. Med.*, C. XXXVI., p. 211) and Calabar bean (BEZOLD and GÖTZ, *Med. Ctrbl.*, 1867, p. 242) act in a similar manner. According to TRAUBE an habitual use of alcohol and simultaneous strong exertion of the muscles, also the excessive use of tobacco, diminish the *tonus* of the arterial muscles, and thus the flow out of the aortic system, and causes chronic endarteritis.

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* BROWN-SÉQUARD'S experiments were contemporaneous with BERNARD'S (1852). B.-S. advanced the theory of vaso-motor action. See LONGET, *Traité de Physiologie*, t. III., p. 612. Paris, 1869.—[ED.]

In a REFLEX MANNER the arterial tonus is reduced or increased : generally by irritation of the central end of the depressor nerve, as well as by section of the splanchnic nerve (the vaso-motor nerve of the vessels of the abdomen) ; locally, in an arterial district, by irritation of the sensory nerves of the corresponding region. The latter reflex excitation is, in healthy bodies, in uninterrupted activity.

The size of vascular regions affected by irritation of sensory nerves depends upon the point at which it is applied. The effect of irritation of a sensory nerve does not, as a rule, extend beyond the limit of its peripheric distribution (LOVÉN).

According to NOTHNAGEL (*Virch. Arch.*, XL., p. 203), the arteries of the pia mater contract, by electrical as well as by mechanical irritation of sensory nerves, mostly after irritation of the crural nerve. RIEGEL and JOLLY (*Ib.*, LII., p. 218) did not find this to be constant.

Like the transversely striated muscles of respiration, the vaso-motor system of nerves experiences a periodical innervation from the side of the respiratory nerve-centres in the medulla oblongata. Hence periodical contractions of the muscles of the vessels result, the so-called RESPIRATORY MOVEMENTS OF THE VASCULAR SYSTEM, which are associated with the movements of respiration (HERING, *Wien. Sitzgsber.*, 16th Dec., 1869).

Special vaso-motor nerve-centres exist for the various vascular provinces.

According to SCHULTZ'S experiments, sections and irritations of the cervical sympathetic and spinal cord show no constant influence upon the vessels of the brain. Their nerves probably take their origin within the cranium itself.

Vessels probably possess in their walls nerve-ganglia, which govern their size. This is corroborated in part by the direct influence of the temperature, in part by pathological observation.

The conditions mentioned which influence blood-pressure in an important manner are: every enlargement of the channel is followed by a lowering of the pressure; every contraction, by an elevation of it. The former occurs after section of the spinal cord, and after section of the splanchnics; the latter during irritation of the spinal cord, and during irritation of the splanchnics. The muscles of the small arteries and veins in the whole body, or in a large vascular district, contract by irritation, e.g. of the splanchnic n., whence the arterial blood-pressure increases. For, in the first place, by contraction of the vessels their blood is driven to the right side of the heart with increased velocity, and the right side and secondarily the left side, in a unit of time, contains more blood. In the second place, contraction of the small arteries causes increased resistance at the end of the arterial current; the disproportion between the quantity of blood entering the arteries and the quantity leaving them, in a unit of time, increases considerably; consequently, also, the pressure of the blood in the large arteries increases. Finally, this disproportion is increased by the activity of the heart, increased secondarily in consequence of the elevated intra-cardial blood-pressure. (Investigations of LUDWIG, BEVER, BEZOLD, CYON, and others.)

GOLTZ (l. c.) has already rendered justly prominent the significance of the activity of the vaso-motor nerves, with respect to the velocity of the blood-current.

According to DOGIEL'S investigations on the influence of the nerves upon the circulation of the blood in the lower extremities (*Arch. f. d. ges. Phys.*, 1872, V., p. 130), there appears during irritation of the crural or sciatic nerves a retardation of the blood-current, and an elevation of the blood-pressure in the femoral artery. A prime condition here is the contraction of the transversely striated muscles. Every contraction

produces in the vessels of the lower extremities a fluctuation in the blood-stream, *i.e.*, retarding it ; but this retarded blood-stream in the arteries and veins of a limb is accompanied by an acceleration of the blood-stream in the other and quiet limb. At the same time a slower blood-current has more time for interchange of material ; thus more oxygen is consumed and more carbonic acid is formed. (By this is explained the utility of active and passive gymnastics.)

Excitation of sensory nerves is followed, for the most part, by a reflex contraction of all vessels, and therewith elevation of blood-pressure ; as said above, there appears in the region of distribution of irritated sensory nerves, mostly dilatation of the vessels, and this may give rise to a decrease of blood-pressure. After removal of the cerebral lobes, or after narcotization of animals, there always arises dilatation of vessels only, never contraction ; but this is not true of vessels within the region of distribution of irritated sensory nerves. After extirpation of the cerebral lobes or narcotization, irritation of sensory nerves is followed always by a decrease of blood-pressure, but never to so great a degree as during irritation of the depressor nerve. (CYON, *Büll. d. Petersb. Acad.*, XVI., p. 97, 1871.)

According to SCHIFF, not only the small arteries (LUDWIG-THIRY), but also the large trunks in many, probably in all parts of the body, dilate after section of the cervical portion of the cord. The chief cause of the heart's feebleness and of the diminished blood-pressure lies, consequently, in the increase of volume of the large dilated vessels, which in their spacious channels retain a great quantity of blood, which can no longer return to the heart, and thus is withdrawn from the circulation. Such an animal is therefore relatively anæmic ; blood is wanting, because a great quantity of it is retained at the periphery.

According to PICK (*Arch. f. Anat. Phys. u. wiss. Med.*, 1872, p. 563), the intensity and quickness of appearance of the reflex contraction of vessels are in direct ratio to the strength of the sensory irritation. Different parts of the body need different degrees of irritation, to call forth an equal contraction of the vessels. The time of contraction and its intensity vary indirectly to the size of the vessel. Diminution in the velocity of the current goes hand in hand with contraction. Contraction mostly follows dilatation, which PICK, differing from LOVÉN, found proportionate to the previous contraction. Dilatation is a sign of exhaustion.

Vaso-motor nerves seldom run an independent course, but are, for the most part, mixed with other motor or sensory nerves, going with them a greater or less distance, and then branching from them to the vessels. Concerning the distribution of the vaso-motor nerves in single regions and organs of the body, we know with precision very little. In the head, most of the nerves of the vessels travel with the trigeminus; the remainder are furnished by the cervical sympathetic, some also by the facial nerve. The nerves of the vessels of the upper extremities (skin and muscles) pass from the lower cervical portion of the spinal cord through the anterior roots and communicating branches into the thoracic cord of the sympathetic. Those for the lower extremities pass from the dorsal portion of the spinal cord into the sacral cord of the sympathetic ; those for the intestines run in the splanchnic nerves.

While the nerves just described are nerves of contraction, and belong to the sympathetic, there are besides, for isolated parts of the body, NERVES OF DILATATION which arise immediately from cerebro-spinal roots. Nerves of this kind pass in great number in the facial nerve to the mucous, lachrymal, and salivary glands. After irritation of the chorda tympani, there is an active determination of blood to the submaxillary glands; the veins are filled to excess with bright red blood. To this class belong the *nervi erigentes*, irritation of which causes an increased and accelerated flow of blood to erectile tissues ; the blood flowing out after having filled the latter tissue is bright red. Irritation of these nerves causes erection of the penis.

The NERVES SUPPLYING the VEINS are anatomically but little known ; but physiological observations testify to the presence of the so-called TONUS OF THE VEINS. The latter, like that of the arteries, is influenced by the great nerve-

centres. Paralysis of the *tonus* in a large vascular region is, from purely mechanical reasons, followed by a lowering of the heart's action. Destruction of the brain and spinal cord arrests, after a time, the circulation, because with a loss of the *tonus* of the vessels the heart's action becomes inefficacious, for the *vis-a-tergo* which fills the diastolic heart is the tension in the veins; if this ceases, the heart remains empty in diastole, and the blood ceases to circulate. The *tonus* is sufficiently increased if either the medulla oblongata or spinal cord is left. Restoration of the circulation after great losses of blood is accomplished in great part by this *tonus*.

Consult GOLTZ (l. c.). The following experiment by GOLTZ (*Arch. f. d. ges. Phys.*, 1871, V., p. 53) shows that the veins like the arteries contract under the influence of the central nervous system and force their contents into the heart: If, from two frogs, the brain and spinal cord are removed from the one and not from the other, and both are suspended perpendicularly and their aortæ cut, scarcely a drop of blood escapes from the former, while 1–2 C. cent. flows from the latter. The mesenteric veins of the former are flaccid and dilated, their contents sink from gravity into the most dependent parts; the veins of the bleeding animal are narrower. BERNSTEIN (*Berl. klin. Wschr.*, 1872, No. 28) places another interpretation on this experiment. In the frog with uninjured spinal cord, the resorbed fluid is driven by contraction of the vessels towards the opening of escape, and space is thus provided for the liquid flowing out of the lymph-sac. If, on the other hand, the spinal cord is destroyed, and with it, therefore, this power. the contents cease their movement in the vessels, and the slight pressure upon the liquid in the lymph-sac is insufficient to overcome the obstruction.

The CAPILLARIES are without nerves. Concerning the influence of the NERVES ON THE LYMPHATICS likewise little is known. It is known that irritation of the nerves accelerates the flow of lymph already in the vessels, but never induces one not present.

Section of the cervical sympathetic. which increases the velocity and tension of the current in the capillaries, but at the same time, by the warming of the tissues. reduces friction in the capillaries, in some cases accelerates the separation of the lymph, in others not. During the reddening of the skin (by injection of tinct. opii into the veins) the blood-pressure in the carotids is often at the same time lowered, and the discharge of lymph is for the most part considerably increased. (LUDWIG.) According to GOLTZ (l. c.) there proceeds from the brain and spinal cord a force by which, after interruption of the circulation of the blood, a more abundant stream of liquid is driven out of the lymph-sacs into the vessels. heart, and aorta. This influence of the central organs on absorption may probably be reflex, through irritation of distant centripetal nerves. What is true of the veins and arteries. with respect to nerve-influence, is probably true also of the contractile lymphatic vessels.

Much less known than the influence of the nerves upon the circulatory apparatus are those MOVEMENTS OF THE HEART AND VESSELS WHICH OCCUR INDEPENDENTLY OF THE NERVES. The movements of the heart, besides being dependent on the vagus and sympathetic and its own ganglion cells, depend upon material changes in its muscular substance, and upon the uninterrupted supply of oxygenated blood: change in its temperature, in its contained oxygen, carbonic acid, etc., induces changes in the movements of the heart. The latter depend, too, on the resistance of the mass of blood, the number of movements increasing with the blood-pressure in the arteries, etc. Thus, in general, we surely know numerous forces which influence the heart's movements, but individually these cannot with certainty be discovered. In the arteries, and probably in the veins, motor phenomena are known, which are independent of nervous influence.

SCHIFF first observed quickly alternating contraction and expansion of the arteries in the ear of a rabbit. These movements were observed by SCHULTZ in the arteries of the pia mater cerebri, and by COHNHEIM in a frog's tongue. They are independent of vaso-motor nerves (for they continue unchanged, after section of all the sympathetic and cerebro-spinal nerves), of the heart's motion, and of respiration. According to BRUNTON (*Arb. aus. d. phys. Inst. zu Leipzig*, 1869, p. 101) such vacillations were also found in all other exposed arterial branches of the skin and connective tissue.

Secale cornutum and ergotine are followed in their use by contraction of the small arteries, and thereby by elevation of blood-pressure : the former is dependent upon a direct influence on the muscular structure of the vessels (BROWN-SÉQUARD). According to BRUNTON, nitrite of amyl acts also directly upon the smooth muscles of the arteries, while it lowers arterial pressure by diminishing the resistance of the circulation. After its inhalation, there immediately arises an intense reddening of the face, with a feeling of great heat in the face and head, strong injection of the conjunctiva, increase of the pulse (20–30 beats), diminution of tension of the radial art., farther on faintness and feelings of distress in the pit of the stomach.

1. ANÆMIA : ISCHÆMIA.

LOCAL ANÆMIA, or ISCHÆMIA, is that condition in which the quantity of blood of a portion of the body, or of one, or many parts of it, is either diminished, or less in proportion to the blood-supply of the rest of the body. In the DEAD BODY an organ is called anæmic if less blood flows from its cut surface, or if fewer points of blood are observed and the vessels are emptier than in the normal state; if the organ appears paler, or, at least, is deprived of its color, for the normal color of organs depends upon the redness of the blood and the proper color of the organs. For this reason, too, not all organs, *e.g.* pigmented lungs, become pale by anæmia. Besides, the size of anæmic organs is diminished, their weight less, with less turgor and resistance.

From examinations of the dead only, it is not always possible to conclude with safety respecting the blood-supply during life and before death : this is demonstrated by many clinical observations, as well as by experiments on animals. Thus by the latter method, ACKERMAN (*Virch. Arch.*, XV., p. 401) showed that death by suffocation is always associated with anæmia of the brain, and that the often perceptible hyperæmia of the brain in the bodies of those who had been suffocated is always the consequence of a mechanical gravitation of the blood, and thus is a phenomenon of death.

THE CAUSES OF LOCAL ANÆMIA sometimes appear alone, sometimes simultaneously with other important conditions, especially with general anæmia (after loss of blood, etc.) and with diminished activity of the heart.

1. MECHANICAL, or PASSIVE ANÆMIA arises most often from PRESSURE, which, caused sometimes by external, sometimes by internal forces, affects either the vessels altogether, especially the arteries, or only the capillaries (pressure upon the veins alone causes venous hyperæmia). Anæmia from pressure on the surface, *e.g.*, occurs from pressure by articles of clothing, bandage, etc.; in internal parts, from strong muscular contractions, accumulated secretions, dropsy, exudations, extravasations, contractions of cicatrices, new-formations of every kind; in the lungs, in marked emphysema; in the intestines, in high degree of meteorism; in the brain, in fractures of the skull with depression, etc. These forces are of especial importance when the organ pressed upon cannot turn aside, as in the closed skull, or when only a trifling avoidance is possible, as in the spinal canal and in the thorax of old people.

2. Anæmia occurs from CONTRACTION or OCCLUSION OF ARTERIES, and

thus is a consequence of arrested blood-supply : ARTERIAL ISCHÆMIA. This form of anæmia arises, besides, through pressure on arteries, especially in places where avoidance of it is impossible (e.g., the art. cruralis above the pubes, various arteries beneath firm fasciæ), through laceration, ligation, and obliteration of arteries, through autochthonic and embolic thrombi, through inflammations, fatty degeneration, etc., of the arterial wall—especially if a collateral circulation does not sustain the blood-supply.

Here also in part belong many so-called COLLATERAL ANÆMLE, e.g., the collateral anæmia of the brain in expansion of the arteries of the thyroid gland, in paralysis of the splanchnic.

3. IDIOPATHIC, or SPASMODIC ANÆMIA, or ISCHÆMIA arises, sometimes from direct influences, e.g. cold, upon the arterial muscles themselves, or upon the capillaries; sometimes through contraction of the arterial muscles in consequence of an irritation or excitation of the sympathetic. The latter occurs at the centre of the vaso-motor nerves, in their course or at their extremities; it happens directly, or in a reflex manner. Here belong: emotions of a depressing nature, as terror, fear, grief, expectation; excited passions, as anger; many convulsions, local as well as general (e.g., so-called reflex epilepsy); the first stage of ague; many paralyses (limbs paralyzed for a long time are mostly pale, cool, their pulse smaller and less distinct); many hyperæsthesiæ; electricity; perhaps the habitual use of alcohol and intemperate tobacco smoking (see p. 161); many medicaments, means for arrest of blood-flow, or styptics, particularly lead, ergot, the sulphates of iron, zinc, copper, etc., perhaps also tannin and the mineral acids; some narcotics, to wit, opium; digitalis.

BROWN-SÉQUARD first demonstrated, that by electric irritation of the sympathetic, conditions opposite to those caused by its division occurred, but more slowly : namely, contraction of the vessels, paleness and lowering of the temperature of the part.
STRICKER (l. c.) observed the almost entire closure of many capillaries (perhaps only young ones) after chemical and electrical irritations. The contracted capillaries were so pale, their contours so ill-defined, that they could hardly be distinguished from the surrounding tissue. This is independent of the nerves. Similar conditions occur probably during the action of many poisons, in mucous membranes brought in contact with the poison. An affection of the œsophagus resulting from the action of caustic alkalies, seen by myself, supports this. (NAGER, Arch. d. Heilk., XIII., p. 221.)
Among the medicaments referred to, some especially are frequently employed to induce local or general anæmia. To the former belong the so-called styptics ; to the latter, especially ergot (see p. 165) and digitalis. The latter, after injection of strong doses, causes a contraction of small arteries, e g., of the mesentery, even complete closure of some, and thereby an increase of arterial blood-pressure.
According to DUBOIS-REYMOND (Arch. f. Anat., u. s. w., 1860, p. 461), those cases of migraine in which the affected half of the head is pale, etc., depend upon a tetanus of the muscles of the vessels of the part, so-called hemicrania sympathico-tonica. With the abatement of pain the affected ear reddens and becomes subjectively and objectively warmer, in consequence of the fatigue of the arterial muscles.
TRAUBE (D. Klin., 1864, Nr. 17) accounts for all febrile phenomena, by assuming a tetanus of the small arteries, chiefly of the small vessels of the body, abundantly provided with muscle-fibres. (See FEVER.)

Along with anæmia of one part of the body, there is always found hyperæmia of one or more other parts : COLLATERAL or COMPENSATORY HYPERÆMIA. Collateral hyperæmia occurs sometimes only in the immediate neighborhood of anæmic parts (the so-called hyperæmic area around inflammatory or exudation area, and new-formations), sometimes at a greater distance from

them, as in hyperæmia of the upper lobes of the lung, in anæmia of the lower from pressure, etc. ; hyperæmia of the brain, lungs, etc., in anæmia of the extremities. Sometimes it affects the same organ, parts of which are anæmic ; sometimes it affects organs at a distance (e.g., in the action of intense cold, in the cold stage of ague). Its extension is quite the same as that of anæmia if that of the latter is small, so also for the most part is that of the former ; if anæmia affect the whole skin, or a large portion of the intestines, hyperæmia also can affect many internal organs. Collateral hyperæmia is sometimes arterial, when arterial blood flows out of the vessels in the vicinity of the anæmic part into the latter ; sometimes venous, when venous blood pours into the empty capillaries and veins, behind the contracted arteries, the lateral pressure being diminished. Collateral hyperæmia sometimes lasts long, sometimes it passes away quickly, when the blood is not long retained in the vicinity of the anæmic part, but is quickly distributed in the general humors.

THE SYMPTOMS OF ANÆMIA are PALENESS, LOWER TEMPERATURE, and DIMINISHED FUNCTION of the parts affected. They are explained, partly by the diminished quantity of blood, partly by retardation of the blood-current. These symptoms are known with certainty, especially in external parts, especially the skin, in the muscles, in the peripheric and central nervous system. Besides, they vary greatly, according to the degree of the anæmia, its extension, and, at least in some organs (especially the brain), according to its origin ; also its seat and extent of the collateral hyperæmia, etc.

PELECHIN (*Virch. Arch.*, 1869, XLV., p. 417) has experimentally, and in surgical cases investigated the influence of distant ligation of main arterial branches upon the corresponding capillary and venous circulation. After ligation of large healthy arteries the circulation is arrested only where there is present no arterial passage for the blood circulation. In all other cases the circulation remains uninterrupted, with the only effect of diminishing for a short time the quantity of blood, and the rapidity of its circulation. The phenomena of *stasis* are very marked only in the first case, and appear in warm-blooded animals in much smaller proportion, on account of the very small channels through which regurgitation is possible, since the larger veins are provided with valves.

According to SAVIOTTI (*Virch. Arch.*, L., p. 592), the circulation in the web-membrane is retarded after closure of the femoral artery ; neither in the arteries, nor in the veins are the central column of blood-corpuscles and the peripheric serous zone to be distinguished ; rather, the channel of the vessels is uniformly filled by a mass which consists of isolated blood-globules floating in serum. The channel is filled full in the capillaries and small veins, and the retardation of the circulation in them is greater than in the large vessels ; sometimes the blood moves with extreme sluggishness ; the marginal zones are not present. The circulation gradually becomes quicker again, and S. saw it restored to its normal condition 36 hours after ligation. Irritation of the web-membrane here acts just as in the open femoral artery.

Consult also SAMUEL (*Virch. Arch.*, LI., p. 41) on the influence of ligation of the arteries upon the origin and course of gangrene and inflammation.

H. NASSE (*Unters. üb die Einflüsse, welche die Lymphbildung beherrschen*, 1871) finds an increase of the lymph-current (24–40 per cent.) after ligature of the carotids The watery contents increase with the decrease in the quantity of lymph.

The DURATION of ANÆMIA is, according to its cause, sometimes short, lasting seconds and minutes, sometimes longer. Upon this depend in great part the results. They are as various in short duration, as the organs (the skin contrasting with the brain). In longer duration, on the contrary, or in complete anæmia appearing suddenly, the nutrition of the part is lessened, even when the anæmia affects the vessels only with respect to their function ; it gives rise to atrophy of various forms, even gangrene.

In ANÆMIA OF THE SKIN, it appears white or faded, which in the absence

of other abnormal colorings of the skin is certainly striking; it appears to
have lost somewhat in volume (unless complications, as dropsy, have arisen).
The sick person, as well as the physician, feels the skin to be colder. Its
secretion is diminished; it is dry and, for the most part, without lustre.
ANÆMIA OF THE CUTANEOUS NERVES is manifested by diminished functions
of those nerves: pale, *e.g.*, chilled parts of the skin feel harder, or give the
subjective feeling of numbness.   Operations on such parts are less painful
(so-called local anæsthesia).

Anæmia of the skin is shown most clearly during the action of low temperatures
(air or water); the skin appears pale, but from long duration of cold it becomes blue.
The latter arises from the fact that by the retardation of the blood-current the
blood-corpuscles take up more carbonic acid than normal.
  According to ALSBERG (*Marb. Diss.*, 1853), anæmia (and hyperæmia) of the skin is
attended by a diminished sense of distance.   The sense of temperature is blunted by
hyperæmia, lessened by anæmia.   If the finger is held for a long time in ice-water,
well-known sharp pains result.   If, on the other hand, it is held in cold alcohol, even
of —5° C., no pain is felt, while the touch is still retained.   Glycerine acts in a
similar manner, while ether gives rise to the same pains as ice-water.   This physio-
logically important fact of an artificial separation of the sense of touch from the
feeling of pain, is also of value surgically (HORVATH, *Med. Ctrlbl.*, 1873. Nr. 14).
  NOTHNAGEL (*D. Arch. f. kl. Med.*, 1865, II., p. 173) describes a neurosis of the
hands and fore-arms dependent on arterial cramp, which consisted in a feeling of
numbness and tingling or cutting pains, always with a disagreeable sense of cold,
with diminished sense of touch, and little or no disturbance of motility.   The fingers
and hands were pale, and from $\frac{1}{2}$–2 C. colder.   The phenomena were sometimes
most marked in the morning after rising.   Warmth moderated them; likewise irri-
tants to the skin (rubbing, but especially the constant current).   Not infrequently
similar and sometimes painful cramps affect smaller localities, *e.g.*, the ends of the
fingers, limited portions of one or many fingers.   They arise quickly, and disappear
quickly, or, for the most part, slowly, their duration lasting sometimes weeks and
months.

ANÆMIA OF THE VOLUNTARY MUSCLES, of slight degree, is known by dimin-
ished contractility, stiffness and numbness; if the anæmia is in high degree
and arises suddenly, it is followed by complete paralysis of the muscles
(just as in the lower half of the body after ligation of the abdominal aorta,
in the extremities after ligation of different arteries).

According to KÜHNE (*Königsb. Ztschr.*, 1867), the affected muscles, in compres-
sion of the abdominal aorta, remain a long time transparent, if they have lost also
their power of contraction; the latter returns with the return of the circulation.
If the muscle-substance is clouded (true *post mortem* rigidity), their irritability does
not return after removal of the ligature.   ROSENTHAL (*Wien. med. Jahrb.*, 1872,
p. 404) found the electro-muscular contractility destroyed, about two hours after
closure of the iliac and femoral arteries.   After removal of the obstruction, con-
tractility was gradually restored.

The phenomena of ANÆMIA OF THE MUSCLE OF THE HEART are as yet
but little known.

BEZOLD (*Med. Ctrlbl.*, 1857, Nr. 23) closed with forceps the coronary arteries of
the heart, after previous section of the n. vagi, cervical sympathetics, and the cervical
portion of the cord.   After 10–15 seconds the heart-beats became less frequent,
after $\frac{1}{2}$–$\frac{3}{4}$ minutes irregular, after 1–$1\frac{1}{2}$ minutes the ventricles were completely re-
laxed.   After removal of the obstruction, the pulsations began again and soon
became perfectly regular.

ANÆMIA OF SMOOTH MUSCLE-FIBRES has as yet hardly been considered.

According to OSER and SCHLESINGER (*Med. Ctrlbl.*, 1871, Nr. 52. *Oestr. Jahrb.*, 1872, p. 57), irritation of the central nervous system through interruption of the respiration, through acute anæmia, or through interruption of the arterial blood-supply, gives rise after a few (10–30, or 80–120) seconds, to a general contraction of the uterus (not impregnated). The irritation is communicated through the spinal cord. (The blood of suffocation, if it has its origin in suspension of the respiration or compression of the aorta, likewise gives rise, only later, to a general uterine movement.)

ANÆMIA OF THE BRAIN, in its highest grades, if general in extent and of very quick origin, as from ligation of all four of the cerebral arteries, is followed by loss of consciousness, of voluntary movement, of sensibility to irritants, by retardation of the respiration, by acceleration of the pulse, dilatation of the pupils, convulsions,—thus resembling an attack of epilepsy or eclampsia. Lighter grades of general cerebral anæmia are probably, for the most part, the causes of fainting-fits, which affect those who had been very sick or are convalescent, during their efforts to sit up in bed, stand up, etc. After ligation of one carotid, or after total embolism of it or of an *art. fossæ Sylvii*, there often arises sudden paralysis of the opposite half of the body. In the less sudden appearance of anæmia, and in individuals of different ages, the symptoms differ and its diagnosis from hyperæmia often becomes difficult. Anæmia of single parts of the medulla oblongata is of especial importance, because of the many cranial nerves which arise therefrom, especially the vagi, and because of the influence of these nerves on cardiac and respiratory movements. Sometimes anæmia of separate parts of the brain, and hyperæmia of other parts (not merely of those in the immediate neighborhood of those affected by the former), occur at the same time and give rise to the most complex symptomatology, particularly that of pressure simultaneously with that of irritation. Anæmia of the brain-substance and similar affections of the meninges cannot be separated. Anæmia of the membranes and of most external parts of the brain are, usually, simultaneous.

The acceleration of the pulse (A. COOPER), following closure of the carotids, depends, according to Mosso (*L'Imparz*, 1872, XII., Nr. 17), upon an irritation in part of the vaso-motor nerves, in part upon that of the nerves which preside over the acceleration of the pulse. The anæmia does not act as the irritant, but the absence of the circulation. M. found, that closure of the common carotids exerted a less intense effect than that of the internal carotid ; also that after compression of the common carotids the blood changes its direction in the internal carotid, and flows into the external carotid.

KUSSMAUL and TENNER (*Moleschott's Unters. z. Naturl.*, 1857, III., 1), by a series of experiments on rabbits, with regard to the origin and nature of epileptoid convulsions in hæmorrhage, as well as of epilepsy in particular, obtained important results. Convulsions, which appear from hæmorrhage in warm-blooded animals and man, resemble those observed in epilepsy. Similar convulsions appear, if the brain has suddenly been robbed of its red blood, as by ligature of the great arteries of the neck. (Also, when arterial blood quickly assumes the character of venous, as by ligature of the trachea.) Probably the appearance of convulsions in these cases depends upon the suddenly interrupted nutrition of the brain (not upon changed conditions of pressure, to which the brain is subjected). Epileptic convulsions have their central focus in the excitable regions of the brain, which lie BEHIND THE OPTIC THALAMI. Anæmia of the parts of the brain lying anterior to the crura, gives rise in man to loss of consciousness, insensibility and paralysis. The blood of the cranial cavity is greater in quantity after ligature of the arteries than after bleeding ; the want of blood always affects especially the small arteries, capillaries and smallest veins. [See K. and T. *on Epileptiform Convulsions from Hæmorrhage.* New Syd. Soc. Trans., Lond. 1859.—ED.]

According to SCHULTZ (*Petersb. med. Ztschr.*, 1870, I. H., p. 64), the iris and fissure of the lids at first contract after ligature of the carotid and vertebral arteries ; the

lids close spasmodically; the animals are unconscious and show no reaction to external irritants; the eye-balls are drawn back in the orbits, and turned upward and outward; respiration is accelerated.   After 10–20 minutes (?), the respiratory movements become slower, the cervical muscles are paralyzed, the head drops upon the breast, the animal bends over, the pupils dilate, and the eyes become prominent. Then tonic contractions of the cervical muscles and general convulsions appear. The extremities contract in clonic form; then the convulsions become more tetanic, and finally disappear altogether.   These attacks last ½–2 minutes.   After a short pause, then begins a second, and third attack, but always weaker and shorter than before.   If the ligature be removed, respiration quickens, and consciousness returns. Microscopical examination, if carotids and vertebrals are simultaneously ligated, shows a distinct paleness of the cerebral vessels, a distinct movement of the blood-corpuscles in the small arteries, the blood-movement appears in the veins, the mass of blood-corpuscles loses in density.

NOTHNAGEL (l. c.), from experiments, by which he observed the vessels of the pia-mater through a trephine-hole in the skull, thinks that many epileptic attacks have their origin in a reflex contraction of the cerebral vessels (with these the vessels of the pia have a common origin) in consequence of irritation of peripheric sensory nerves.   Many cases of so-called reflex epilepsy testify to this.   (See p. 162.)

The signs of so-called compression of the brain, besides which there often exist at the same time concussion and contusion (in consequence of fractures of the skull with depression, hæmorrhage, etc.), are, in general, loss of consciousness, sleepiness (or sopor, coma, stupor, etc.), normal cardiac and respiratory movements or retardation of both, etc.   According to PAGENSTECHER, a pressure upon the brain, sufficient to destroy life, must amount to about 180 mm. quicksilver, and thus equal the blood-pressure in the carotids.   Consult text-books on surgery.   Also the experimental investigations of HEGELMAYER, *Die Athembewegungen beim Hirndruck*, Tüb. Diss., 1859.   LEYDEN, *Virch. Arch.*, 1865, XXXVII., p. 519.   JOLLY, *Unters. üb. d. Gehirndruck u. über die Blutbewegung im Schädel*, Würzburg, 1871. PAGENSTECHER, *Exper. u. Studien über Gehirndruck*, Heidelberg. 1871.

SCHIFF'S experiment demonstrates the crossed conduction of sensations.   During compression of the carotids near the larynx, there appear formication, slight feeling of warmth in the extremities, and half of the head of the other side.   During compression of longer duration, there arises decrease of sensibility to pain and pressure in the parts of the opposite half of the body.

According to DURHAM (*Guy's Hosp. Rep.*, 1860, VI., p. 149), anæmia of the brain is the normal condition in sleep.   This is shown by examination of the brain through a hole in the skull made by a trephine, during sleep from chloroform; as soon as the animal awakes, the surface of the brain reddens and bulges out of the cranial opening.   According to OBERSTEINER (*Allg. Ztschr. f. Psych.*, 1872, XXIX., p. 224), the accumulation of acids arising from fatiguing activity in nerves (FUNKE) and brain (HEIDENHAIN) causes fatigue of the brain and sleep: and indeed anæmia acts like hyperæmia, etc.   [Consult, W. A. HAMMOND, *Sleep and its Derangements*, Phila., 1869.—ED.]

ANÆMIA OF THE SPINAL CORD gives rise to paralysis of sensation and motion of all the nerves of the extremities given off below the part affected (most so-called paraplegiæ), also of those of the trunk, respiratory muscles, bladder, and contraction of the pupils, according to the extent of the anæmia.

ISCHÆMIC PARALYSES are those in which the motor affection of innervation is dependent on a cutting off of the arterial blood supply in certain parts of the nervous system.

STENON already in 1667 demonstrated the same fact, by compressing or ligating the abdominal aorta in rabbits, beneath the point at which the renal arteries are given off: after a few minutes there appeared complete paralysis of the hind extremities, which in compression of short duration, after a short time, again passes away.   The paralysis did not proceed from the muscles, as STENON and others believed, but from experiments by LONGET, SCHIFF, SCHIFFER, ETC., it has its foundation in the arrested excitability of the spinal cord and peripheric nerves: closure of the spinal branches of the lumbar arteries, entering through the intervertebral foramina, is followed by an anæmia of the spinal cord, probably chiefly of the gray substance.

KUSSMAUL (*Berl. klin. Wchnschr.*, 1872, Nr. 37) found in a case of so-called tetany (CORVISART'S), which was characterized by attacks of tonic convulsions of many symmetrical muscles of all four extremities, the signs determined by TROUS-SEAU, that, to wit, in the intermediate parts free from convulsions, convulsions appear as soon as pressure is exerted upon the principal artery of the member.

The secretion of GLANDULAR ORGANS is diminished in consequence of ANÆMIA, and probably also changed.

In the KIDNEYS there arises, *e.g.*, in incomplete filling of the left side of the heart and incomplete filling of the renal arteries, a diminution in the quantity of the urine; the urine is deficient in water, concentrated, dark, urates easily precipitate in it, because they are relatively increased. The same thing is observed when a large quantity of water is excreted through the skin (in great sweats). In the LIVER, the separation of bile is diminished after closure of the portal vein; and yet it stops completely if the hepatic arteries also are obstructed. A diminution of secretion also occurs in anæmia of the GLANDS OF THE MUCOUS MEMBRANES.

That local anæmia diminishes the secretion of bile, is shown by the experiments of HEIDENHAIN (Reizung der Gefässnerven), PFLÜGER (directe electrische Reizung der Leber), and RANKE (gesteigerte Arbeitsleistung der Körpermusculatur).

Concerning ANÆMIA OF THE VESSEL-WALL, see Embolism.

GENERAL PHENOMENA, in consequence of anæmia, occur only when the latter is very extended (*e.g.*, in common coldness, as after marked and sudden cooling of the surface of the body, and in intermittent fever, where anæmia affects the whole skin), or when important nerve-centres are the seat of anæmia, etc. General phenomena then have their foundation in compensatory hyperæmia of other important organs, especially of the brain and lungs, or in changes in the heart's action, blood-pressure, etc.

The general consequences of irritation of the splanchnic nerves are, physi-logically, known with certainty. After irritation of the cut splanchnic nerve, there arises an ANÆMIA OF THE ABDOMINAL VESSELS (since every muscular movement, every inspiration diminishes their contents), and considerable INCREASE of BLOOD-PRESSURE. By irritation of the peripheric extremity of the splanchnic, the PULSE becomes SLOWER; by irritation of the central end, the pulse is MOSTLY ACCELERATED. With respect to these experiments we have only isolated pathological examples: best known is the large and slow pulse in many cramped states of some abdominal organs.

Ligature of the carotids causes an increase of blood-pressure, and, in consequence of the cerebral anæmia, an increase in number of heart-beats. MOSSO found, that increase of blood-pressure following closure of a carotid is to that following closure of both iliacs as 4:1. Here the curve of the tracing, steep and sudden, kept at an almost equal height, and, with the removal of the ligature, suddenly returned to the normal state; then it was irregular, and later, gradually disappeared. A greater frequency of pulse occurs also from like causes, in the change from a horizontal to a vertical position (MANTEGAZZA, *Gazz. med. ital. Lomb.*, 1868, pp. 337, 362).

Blood-pressure rises, by irritation of the spinal cord and consecutive contraction of almost all the small arteries of the body, with or without destruction of almost all the cardiac nerves.

SCZELKOW (*Ztschr. f. rat. Med.*, 1863, XVII., p. 120) found a lowering of the temperature of the body and a diminution of excreted carbonic acid in rabbits, whose abdominal aorta he had compressed.

FAINTING during the presence of PLEURITIC EXUDATIONS is, according to TROUSSEAU, dependent upon displacement of the heart from its natural position, and the resulting torsion of the great vessels connected with it, especially the aorta. BARTELS (*Arch. f. klin. Med.*, IV., p. 263) seeks his explanation in this: the large venous trunks, and especially the vena cava ascendens, suffer, by the heart's displacement, an almost right-angular bending, where the cava passes through the middle tendon of the diaphragm to enter the pericardium, and where it is firmly attached to the borders of the quadrilateral foramen.

2. HYPERÆMIA.

LOCAL HYPERÆMIA is the term applied to the increase of the blood contained in more or less dilated and, for the most part, also lengthened vessels of an organ or of a part of the body, so that the normal fluctuations of the quantity of blood are exceeded.

Local hyperæmia is active or passive. Those hyperæmiæ are called ACTIVE which appear in consequence of relaxation of the vessels, so that the usual blood-pressure alone causes a more excessive filling of them. On this account, this form of hyperæmia is known also as ATONIC, RELAXATIVE, PARALYTIC, or, because it most often acts upon the arteries, ARTERIAL. Finally, of equal significance is the name CONGESTION, etc. Those hyperæmiæ are called PASSIVE, whose principal cause is the increase of resistances; since here a mechanical force is often interposed, it is also called MECHANICAL, or, since this force most often lies in the veins, VENOUS. In both forms of hyperæmia there is present a dilatation of the finer vessels; this dilatation is primary in active hyperæmia, in the passive form, secondary.

COLLATERAL, OR COMPENSATORY HYPERÆMIA is almost always active or congestive, and occurs only with partial anæmia. It occurs, if the blood, arrested in its course by an obstruction, e.g., by ligature, etc., seeks other, near or distant channels. (See p. 166.)

How different active and passive hyperæmiæ are, according to cause, symptoms, etc., is best observed as they affect a single organ, e.g., the kidneys. ACTIVE RENAL HYPERÆMIA arises from excessive filling of the vascular system, as after abundant drinks; from hypertrophy of the left ventricle; from the use of diuretics; from compression, etc., of the abdominal aorta below the renal arteries, also from obstruction to the circulation in the capillaries of the skin in the cold stage of various diseases (so-called COLLATERAL hyperæmia), etc. In all these cases the hyperæmia affects chiefly those parts of the kidneys whose blood has to overcome the greater resistance in the arteries which supply the Malpighian bodies. The chief symptom is an increased secretion of urine; the urine is more dilute, paler, and of diminished specific gravity. If the blood-pressure in the Malpighian bodies becomes still greater the urine is albuminous, or even bloody. PASSIVE HYPERÆMIA OF THE KIDNEYS has its origin in many diseases of the heart, in contraction of the vena cava and of the renal veins, in various diseases of the lungs, etc. Here, the blood increases in the veins and capillaries, less in the vessels belonging to the Malpighian bodies. It is noteworthy that there is always present a low tension of the blood in the renal arteries and their branches, and a high tension of the blood in the capillaries. The chief symptoms are, diminished urinary secretion, increase of its specific gravity and of its solid constituents, and the presence of albumen, blood, and casts.

Both active and passive hyperæmiæ may be ACUTE or CHRONIC. The former are more often acute, the latter mostly chronic.

The diagnosis of hyperæmia in the DEAD BODY is in many cases altogether impossible, since active hyperæmia of external parts (as of the skin in scarlet-fever, erysipelas, etc.), of external mucous membranes, as well, probably, as that of many internal organs also, disappears entirely, or almost entirely, for reasons not yet sufficiently known, with the appearance of death. With respect to single organs, no permanent advance has been made, since a safe opinion is reached only through long experience in autopsies, and since in each special case respect must be had to the blood-contents of the whole body. In the cadaver, hyperæmia of an organ is generally much oftener assumed to exist than is true, especially because most form their opinion of the blood-contents of single organs in the bodies

of those chiefly who have been affected with acute or chronic anæmic diseases.

A hyperæmic organ in the dead body is darker colored, from light to the darkest red, without any appearance of the normal coloring. Its size is somewhat increased, it feels somewhat firmer, but in reality with less consistency; it is heavier. More blood than usual flows from its cut surface. Hyperæmia chiefly affects the capillaries, so that the organ has a uniform redness, withou the individual vessels being seen by the naked eye. The capillaries have an especial arrangement, as appears from their injection: e.g., finely punctated in the villi of the mucous membrane, in the Malpighian bodies of the kidneys, in streaks in the muscles, etc. It is impossible to distinguish between the appearances dependent on injection of the arteries and those dependent on injection of the veins, except that in venous hyperæmia there is present a bluish coloring. If the small veins and arteries are overfull of blood, the surface appears injected with a red material, forms a red network, or assumes a form differing in accordance with the disposition of the vessels of the part. The remaining tissues of a hyperæmic part are diminished in size in correspondence with the increase of blood, etc.

An increase of the quantity of blood is impossible, without extension of the district supplied, therefore the vessels are found always dilated, also for the most part elongated, and, on this account, abnormally tortuous; the dilatation is sometimes uniform, sometimes spindle-shaped or pouched. The blood in the fine vessels is mostly richer than usual in blood-corpuscles; the corpuscles lie so close to one another, that the vessels often appear filled with an uniform dark red mass, and the individual corpuscles can no longer be distinguished.

In a case of very marked hyperæmia of the lungs in well-developed leucocythæmia, the lungs appeared flaccid, and as if in the stage of gray hepatization.

A. ACTIVE, OR ARTERIAL HYPERÆMIA : CONGESTION.

(Relaxative or paralytic hyperæmia. Fluxion. Turgor. Orgasmus. Determination of blood.)

ACTIVE HYPERÆMIA consists in an increased, and at the same time for the most part accelerated, flow of blood into the arteries of a part, because either the blood-pressure of that part is increased, or because its resistances in proportion to the force of the blood are diminished.

The quantity of blood in a part depends upon the number and size of the afferent arteries, as well as upon the velocity of the current within them; the number of the arteries is constant; their size is subject to the influence of the nerves; the velocity of the current is dependent upon the greater or less distance from the heart, and the number and angle of the branches, etc.

That hyperæmia is FUNCTIONAL, which probably all organs show during their activity: the muscles, etc., during motion, the stomach and intestines during digestion, etc.

According to RANKE (*Die Blutvertheilung und der Thätigkeitswechsel der Organe*, 1871), the whole amount of the blood of the organism is primarily diminished by the activity of the muscles, and this diminution is proportionate to the muscular action. The habit of muscular labor is followed secondarily by increased amount of the whole

blood. Long continuous rest reduces it. In animals at rest, there is found about one-quarter of the amount of the blood in the heart and great vessels, one-quarter in the muscles, liver, and remaining organs. The motor apparatus of tetanized rabbits during muscular contraction contain a mean of about 29.4 per cent. of the whole amount of blood more than the same apparatus of rabbits during rest. The portion of the amount of blood, which is contained in the motor apparatus in the quiet state, is during contraction increased by a mean of 36.6 per cent. up to 66.0, *i.e.*, an increase of 80 per cent. During tetanus there is found a clear diminution of the flow of bile, as well as of the urine discharged by the ureters.

The above facts explain the long-known hygienic and therapeutic uses of active and passive muscular movements, as well as their effects in various affections, *e.g.*, congestive states of the brain, and of the abdominal organs.

The CAUSES of ACTIVE HYPERÆMIA are:

1. COMPENSATORY INCREASE OF THE COLLATERAL PRESSURE LATERALLY FROM OBSTRUCTIONS IN THE BLOOD-STREAM: so-called COLLATERAL HYPERÆMIA.

The obstruction may lie in the arteries, in the capillaries, and in the veins; in the last case there arise simultaneously phenomena of both active and passive hyperæmia. Examples of this kind of collateral hyperæmia frequently occur also under physiological conditions. If an artery be ligated (the best for experimentation is the mesenteric; surgically in amputations), small branches extend out laterally, and the blood flows through them with stronger pressure and increased velocity, and through the capillaries into the veins: small, formerly pulseless arteries, even capillaries, then show a pulsation, which can be seen and felt, and, *e.g.*, in amputations, give rise to remarkably great hæmorrhage; parts of organs, which heretofore were pale, become reddened in greater or less intensity. These conditions of the circulation continue until the excessive stream is distributed among the many lateral branches, and so becomes equalized. Greater obstructions in the capillary system of an organ or part of an organ, as by constricting cicatrices, by new-formations of all kinds, by pressure chiefly, by capillary embolism, in the vicinity of inflamed parts, give rise to neighboring hyperæmia. In marked meteorism, etc., we not infrequently see hyperæmia of other parts, *e.g.*, of the brain. Severe external cold, and the cold stage of fever, offer farther striking examples; while anæmia extends throughout the surface, the blood flows in greater quantity and with greater force into the internal organs, giving rise to hyperæmia of the viscera of the cranium, thorax, and abdomen. (The contrary is seen in the application of Junod's boots; the extremities become filled with blood; then results collateral anæmia of the brain and lungs, with consequent vertigo and shortness of breath.) In the veins, collateral hyperæmia is mostly of little importance, because their anastomoses are very numerous, and their walls thinner and more yielding. Contraction or closure of a small or middle-size vein is unimportant, if its collateral branches be numerous; contraction of the superficial veins is followed by dilatation of the deep veins, and vice-versa. If all the veins of a part be closed, their blood has the same lateral pressure as the afferent arteries; but if only a few veins are impassable, the lateral pressure of those remaining open is increased, and the velocity of the blood is greater.

Collateral hyperæmia has a prominent significance (if we exclude surgical cases, where its importance is at once perceived) especially in many diseases of the lungs, *e.g.*, in thrombosis and embolism of the pulmonary arteries, in infiltrations, emphysema, compression by pleural exudations. It sometimes occasions dyspnœa, as well as death in the early stages, *e.g.*, of pneumonia. In compression of one lung we see in this way collateral hyperæmia of the other; in pulmonary emphysema of the

upper lobes, we find hyperæmia of the lower, and thence bronchitis, etc. Collateral hyperæmia is likewise important in so called granular kidney; here numerous glomeruli and tubules are destroyed, so that the blood flows through the open vessels with greater velocity and under increased pressure. The quantity of the excreted urine is normally great or increased; the urine itself is clear, pale, and of light specific weight. The utility of hot local baths, of local irritations, depends essentially on their producing collateral hyperæmia.

In collateral hyperæmia the BLOOD-CURRENT is sometimes to be found TURNED IN THE OPPOSITE DIRECTION. This is most easily observed in cases of great collateral extension of the epigastric and other veins, in complete closure of the trunk of the vena portæ, or in granular liver.

SAMUEL (*Berl. Ctrlbl.*, 1869, No. 25) has experimentally demonstrated that the nerves exert an influence on the accomplishment of the collateral circulation; it is retarded in proportion to the sensory nerves cut across at the time of ligating the carotid. But if the carotid be ligated, and if at the same time, paralysis of all three sensory nerves (*n. auric. major and minor*, and *auric.-temp.*) and of the cervical sympathetic be induced by section, the collateral circulation will be restored already by the second day.

2. ABSOLUTE DECREASE OF RESISTANCE.

a. Quick REMOVAL OF EXTERNAL PRESSURE. If a part has been for a long time subject, in a normal or abnormal manner, to a certain pressure, the quick removal of the latter occasions an active hyperæmia in that part. As examples: hæmorrhage into emptied Graafian follicles; dry cups and Junod's boots; puncture of hydrocele, of ascites; section of the ocular muscles in operations for squint; that of the cornea in operations for cataract; extirpation of large tumors, which compress vessels; healing of strictures. Deep inspirations during contraction of the glottis, *e.g.*, in laryngeal croup, are followed by rarefaction of the air in the bronchial tubes and air-cells, and thence by hyperæmia.

b. RELAXATION, or PARALYSIS OF THE MUSCLES OF THE WALLS OF THE VESSELS from GREATER WARMTH, or from direct or reflex PARALYSIS OF THE SYMPATHETIC; so-called RELAXATIVE, or PARALYTIC, or ASTHENIC hyperæmia.

EXTERNAL WARMTH gives rise in many cases to hyperæmia; its action in the form of baths, fomentations, etc., is often employed therapeutically. In a similar manner the heat of the blood acts in fever.

PARALYSIS OF THE SYMPATHETIC is direct or reflex.

DIRECT PARALYSIS of the fibres of the sympathetic takes place in their course, at their origin, or at their termination.

SECTION OF THE SYMPATHETIC alone, as it has very often been performed in various parts of the body, for experimental purposes, is one of the most perceptible causes of hyperæmia. (See p. 160.)

Sections of other, mostly MIXED NERVES (*e.g.*, the sciatic, ulnar, etc.), or of purely sensory nerves (*e.g.*, the trigeminus), which have happened experimentally in animals, traumatically or therapeutically in man, act as if these nerves contain vaso-motor fibres. Also pressure upon these nerves, or new-formations in them.

The best known and the most important sections of nerves in experimental pathology have been those of the trigeminus, which, since MAGENDIE (1824), have been frequently repeated. These sections are followed by hyperæmia of the conjunctiva and cornea, of the mucous membrane of the mouth and nose, with consecutive disturbances of nutrition. Many pathological cases also are to be traced to the same causes, or to compression or degeneration of this nerve, but seldom to the same affection of other nerves: so-called DIRECT NEURALGIC HYPERÆMIÆ, *i.e.*, hyperæmia, elevation of temperature, and for the most part also swelling of the same parts, appearing during a neuralgia or remaining behind after its disappearance.

Whether affections of the terminal sympathetic nerves cause hyperæmia, it is for the most part difficult to determine, since many affections of this kind may also be reflex in character. The so-called *aneurysma cirsoideum* (*varix arterialis*) probably belongs to this class. Various AFFECTIONS OF THE BRAIN AND SPINAL CORD give rise to hyperæmia, only through the interposition of the sympathetic. In this relation are known the hyperæmia dependent upon the emotions of a violent kind (fear, anger, passion, sensual desires), and those following injuries and many diseases of the spinal cord, less often of the brain and its meninges.

BUDGE, WALLER, and SCHIFF first demonstrated that injury of the medulla oblongata had the same consequences as section of the sympathetic. In section of a lateral half of the medulla there appeared hyperæmia and increase of temperature of the lower parts of the extremities on the side of the section, of the body, upper arm, and upper part of the thigh on the opposite side (SCHIFF).

REFLEX PARALYSIS OF THE SYMPATHETIC arises most often from irritation of sensory nerves. The dilating action of an irritated sensory nerve does not, for the most part, extend beyond the limit of the region supplied by the affected nerve (p. 162). The reflex act takes place probably in the medulla oblongata. This reflex paralysis of the vaso-motor nerves has been experimentally demonstrated in many vascular regions (*art. auricularis, art. saphena, art. dorsalis penis*).

LOVÉN (*Ber. d. Sächs. Acad.*, 1866, p. 85), who made these experiments, showed further that irritation of the sensory nerves, besides causing dilatation of the arteries, is also followed by a retardation of the heart's action, and that the dilatation of the vessels is often preceded by a contraction of short duration.
According to HERMANN and GANZ (*Arch. f. d. ges. Physiol.*, 1870, III., p. 8), the danger of cold draughts in the heated body lies in the effect of cold upon the *nervi splanchnici* and the resulting elevation of the arterial blood-pressure. Since inspiration, and perhaps still other compensatory processes, prevents in great part this increase of blood-pressure, the danger becomes insignificant. It becomes greater in failure of the compensation, etc.
Perhaps also in this way may be explained the hyperæmia of the intestinal mucous membrane, which frequently follows extensive burns, and which may progress (especially in the duodenum) to hæmorrhage and ulceration.
H. FISCHER (VOLKMANN, *Samml. klin. Vortr.*, 1870, No. 10) seeks to establish surgical SHOCK as a reflex paralysis of the vaso-motor nerves, especially of the splanchnics, dependent upon traumatic concussion. Shock occurs especially after wounds, respiratory concussions and contusions of the thorax, abdomen, testicles; after luxations, after contusions of the bones, after sudden and great losses of blood, after many surgical operations (reduction of large herniæ, ovariotomy, etc.).

The so-called REFLEX NEURALGIC HYPERÆMIA, arising from similar transient or continuous causes, or occurring during the progress of neuralgia, has long been known, but not explained. Here we have hyperæmia of the mucous membrane of the nose in irritation of it; that of the conjunctiva in over-exertion of the retina, in tooth-ache; hyperæmiæ of the head after meals; priapism during irritation of the urethra by gonorrhœal poison; congestions of the liver from spirituous liquors and strong spices; pulmonary hyperæmia from the respiration of very cold, still oftener of very hot air, as well as of air suspending irritating substances, as dust of all kinds.

Many articles of food, medicaments and poisons, act directly, or in a reflex manner on the sympathetic: thus alcohol, coffee, tobacco, opium, atropia.

The action of the so-called IRRITANTS is probably to be explained in this manner. Among these are many with which we are acquainted, like cold,

which tend to produce, first, a contraction of the smaller vessels ; then, longer employed, a dilatation. Electric currents generally contract the vessels ; but strong currents especially, as well as weaker ones acting for a long time, dilate them. The same is true of volatile and strong materials, which produce redness of the skin (mustard, cantharides, acids, ammonia).

O. NEUMANN (*Prag. Vjschr.*, 1863, I., p. 1 ; 1867, I., p. 133), as well as MANTE-GAZZA (1866), have examined the physiological action of irritants of the skin (so-called epispastics).

That many CONTAGIONS and MIASMS are followed by congestions of certain organs is a subject which belongs to special pathology. It is an interesting fact that these congestions vary in different epidemics, according to intensity, extension, locality, etc., *e.g.* in scarlet fever.

In many cases hyperæmia of a part follows anæmia of the same part : especially is this true of anæmiæ dependent upon external cold, as well as upon excitation of the sympathetic. This is most favorably demonstrated in the production of local anæsthesia by means of the ether spray. The cause here lies partly in the removal of the influence of the nerves, partly in an exhaustion of the smooth muscle fibres.

c. NUTRITIVE DISTURBANCES IN THE WALLS OF THE VESSELS, observed in their lighter forms in the vicinity of wounds, in inflamed parts, as well as in their more marked forms in chronic arteritis, fatty degeneration of the muscular coat, etc., as is often the case in old persons. Accelerated movements of the heart, from whatever cause (movements of the body, the use of spirituous liquors, emotions), are then followed by hyperæmiæ in the regions of less resistance.

According to VIRCHOW, intercurrent attacks of vertigo, loss of consciousness, fainting, are, in old people, often the consequences of this form of hyperæmia.

The causes of many tolerably constant, and symptomatically not unimportant hyperæmiæ are unknown : thus the circumscribed redness and increased warmth of one cheek in pneumonia, mostly on the same side as the diseased lung, the circumscribed redness and elevated temperature of both cheeks in tuberculosis, etc.

The causes of the HABITUAL TENDENCY TO CONGESTIONS which many individuals present, with respect to certain organs, *e.g.* the brain, lungs, liver, kidneys, thyroid gland, are unknown. They may depend upon a low power of resistance of the arteries and capillaries, as well as upon special conditions of the sympathetic, or sensory nerves. Likewise is it unknown why in hypertrophy of the left side of the heart congestions often appear in various organs. The manifold congestive states are also worthy of notice, which appear in girls before the first appearance of the menses, or before the appearance of each menstrual act, as well as those which appear in the climacteric years : in the former the thyroid body is most often affected ; in the latter, various organs.

THE SYMPTOMS OF ARTERIAL HYPERÆMIA are easily recognized externally in parts exposed to view. And yet a similar behavior, also, in hyperæmia of internal organs can, with the greatest probability, be inferred, especially since a number of internal organs, in the hyperæmic state, have been observed immediately or mediately (by the ophthalmoscope, laryngoscope, etc.) with the naked eye, or by means of the microscope. Their knowledge becomes important from the fact that many affections of daily and hourly occurrence to the physician, for the most part quickly appearing and quickly

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disappearing, depend upon them; and that hyperæmia is the introduction
to many hæmorrhages, dropsies, and especially inflammations.

The symptoms of hyperæmia are partly those which result directly from
the increase and acceleration of the blood-current (injection, redness, pulsa-
tion), partly those which are distant results (elevation of temperature,
swelling, increased nutrition). The last, increased nutrition, results either in
an increase of function (the so-called functional hyperæmia of the muscles,
brain, glandular organs), or in an increase of secretion (skin, kidneys); or,
if of longer duration, in hypertrophy and new-formation (sometimes as fat,
sometimes as true hypertrophy of the muscles, sometimes as heterogeneous
new-formations).

The behavior of the smallest arteries and veins, as well as of the capil-
laries and lymphatics in hyperæmia, is still little known. Dilatation of
the bloodvessels is easily and with certainty established. Doubtless they
become more porous, so that more serum and plasma pass through their
walls, while red and white blood-globules do not, as in inflammation,
usually pass through, or only in insignificant numbers. The plasma-layer,
so-called, perhaps disappears in the smaller arteries and veins, so that red
and white blood-corpuscles fill the whole vessel. The blood at first, from
microscopic observations on the web-membrane and mesentery, flows more
quickly—in consequence of the diminished arterial resistance from dilata-
tion; if the arterioles be considerably dilated, the current will become
slower—in consequence of the increase in size of the channel.

LORTET found in the horse, that the velocity of the blood in one carotid was con-
siderably increased during ligation of the same vessel of the other side. DOGIEL
(see p. 162) could not corroborate this in the dog and rabbit.

According to the usually accepted view, the QUANTITY of LYMPH found in a part of
the body at a given moment increases with the increased blood-supply, as well as
with the hindering of the reflux into the veins and lymphatics; lymphatics are the
chief regulators of the turgor of the tissues. (If this regulation be prevented, œdema
appears.)

According to GOLGI (*Virch. Arch.*, LI., p. 568), the perivascular lymph-spaces of
the brain (which according to G. are connected with those of the pia and indirectly
with those of the arachnoid) are compressed in the more vigorous filling of the blood-
vessels (hyperæmia), but are filled in diminished blood-pressure.

G. ETILJENS (*Beitr. z. Circul. in d. Schädelhöle, Dorp. Diss.*, 1872) injected defibrinated
blood into the carotid of a horse under high pressure, and measured the lymph
flowing in short fixed periods of time from the large cervical lymphatics. With the
beginning of the injection and immediately thereafter, the flow of lymph rose con-
siderably, and indeed so quickly that it could not be assumed that there was an
increased transudation from the bloodvessels into the perivascular spaces, but a
mechanical pressure of the fluid out of the latter. Herein consists the possibility of
a quick equalization, under sudden increase of blood-pressure within the cranial
cavity. Should the increased pressure be of longer duration, an increased transuda-
tion takes place, and with it œdema of the brain, with symptoms of compression.

A stronger filling of the vessels, so-called INJECTION, is the most striking
symptom of congestive hyperæmia. At first the arteries are the vessels
concerned, sometimes also the veins; for the most part then there arises a
close capillary injection. The latter is sometimes circumscribed, sometimes
diffused. Certain organs are more disposed to circumscribed injections,
since their vessels have relatively few anastomoses, *e.g.*, the lungs, spleen,
kidneys; or there are certain parts within the organs which serve as the
seat of congestion, as the small glands of the skin and of the mucous mem-
branes, the Malpighian bodies of the kidneys. Injection is most marked in
clear and transparent organs (conjunctiva, retina), as well as in soft pliable
parts (*e.g.*, in the mucous membranes, lungs, as opposed to fibrous and

osseous tissues).   In opaque parts, *e.g.* the skin, there is found only redness.

The REDDENING of hyperæmic parts is a consequence of the greater quantity of blood in the dilated vessels, as well as of the greater proportion of blood-globules in this blood.   The arrangement of the vessels and relations still unknown give it various forms: it is punctiform in organs which contain papillæ or tufts, streaked in muscles, etc.; it is sometimes spotted, as in measles; sometimes more punctated, as in scarlet fever; sometimes uniform, as in erysipelas.   It is made to disappear by pressure, but on its removal returns again very quickly.   If the hyperæmia remain long the vessels become considerably dilated and the circulation retarded, thus giving a more intense color to the blood-globules, and consequently a bluish-red color to the parts, as is most often seen in parts of the skin which have been chilled: then under pressure there appears at first a brick-red color, later only the bluish-red color reappears.

Partial congestive hyperæmia (in the hand or foot) was seen by HÜTER (*Arch. f. klin. Chir.*, XII., p. 1) in so-called arterial transfusion.

The FEELING OF PULSATION, which the sick often experience in congested parts, is in consequence of the diminished elasticity and tonus of the vessels.   It is especially frequent and troublesome in headache and toothache.   Sometimes the pulsation is objective, *e.g.*, as in *pulsatio epigastrica*. In many cases a pulse is felt also in arteries which do not normally show any pulsation.

The TEMPERATURE of the hyperæmic part rises in consequence of the more vigorous flow of blood into the dilated vessels.   This rise again disappears after previous section of the cervical sympathetic, and after compression or ligation of the supplying arteries.   It does not appear if before section of the sympathetic the carotids and vertebral arteries have been ligated.   The rise in temperature is not merely with respect to the feelings of the sick, whose external parts are accustomed to a lower temperature, because these lose much of their warmth through radiation, but it is also objective, and reaches to 3° C.   For the patient the increase in temperature is sometimes the only and most troublesome symptom, *e.g.*, in congestions of the face.

Experiments of BERNARD, KUSSMAUL and TENNER, VIRCHOW, SCHIFF.

Experimental section of nerves, *e.g.*, of the brachial plexus, of the sciatic, is followed (besides by the loss of motion and sensation) by immediate dilatation of the vessels and increase in temperature (BERNARD, SCHIFF, etc.).   Similar cases from gunshot wounds of the nerves in man with consecutive elevation of temperature were observed in the late American war by WEIR MITCHELL, MOREHOUSE, and KEEN. Most of the cases from human pathology opposed to this, are to be explained by the fact that they came under observation only after a longer time after the reception of the injury; then mostly stagnation-hyperæmia, retardation of the circulation and decrease of temperature were present.

Experimental sections, lacerations, etc., of the upper part of the SPINAL CORD, likewise cause a considerable increase in the temperature of the whole body (or fever).   Spinal paralysis less frequently than those of peripheric origin are followed by rise in temperature, etc.   HUTCHINSON found the lower extremities affected by a pungent heat after injuries in the lower dorsal and lumbar region, their skin dry, the tibial arteries more easily felt, dilated and throbbing; their temperature at first was considerably increased.   LEVIER and COLIN saw similar effects from hæmorrhage and inflammation of the spinal-cord.

In CEREBRAL hemiplegia, a rise in the temperature of the paralyzed is for the most part found at first, however hardly reaching 1° C.   The temperature becomes

normal again with the healing of the hemiplegia. In very long duration of the hemiplegia the same or a diminished temperature is found.

The SWELLING of hyperæmic parts is mostly trifling and is to be seen at once in the skin, visible mucous membranes, thyroid body. It usually appears more marked only after a longer duration of the hyperæmia. It is greater in proportion to the vascularity, softness, and pliability of the tissues, as, *e.g.*, in the face (thickened cheeks from tumors in the gums), in the arch of the palate, in the thyroid body (congestive goitre). The swelling of hyperæmic organs is not infrequently prevented by the surrounding parts; thus the increase in size of the brain by the closed skull, also, in part, that of the liver, spleen, kidneys, etc., by their capsules. The material exuded from the vessels, " exudation of hyperæmia," occurs according to locality, as œdema (collateral œdema), as dropsy, as blennorrhœa, as albuminous urine, as increased wound-secretion, etc. The swelling arises from the dilatation of the capillaries and their greater porosity, in consequence of which more serum or plasma is transuded, than can be carried away by the lymphatics or consumed by transformation into tissue.

The common cases of acute rheumatism of the joints consist in hyperæmia and serous accumulations in the cavities of the joint and in the parts surrounding them. This is demonstrated by examinations in the living, and perhaps also by its quick appearance and disappearance (spontaneous, or after local therapeutic interference, etc.) : autopsies usually furnish negative results.

GRUENHAGEN (*Königsb. med. Ges.*, Nov., 1866) advises that certain painful operations (reduction of strangulated hernia, removal of foreign bodies from the canals of the body) be undertaken where possible only after preceding local anæsthetization (by ice, ether-spray, etc); for repeated irritation of sensitive nerves produces local dilatation of blood-vessels and cramming of the affected tissues with blood.

HÆMORRHAGES worthy of notice appear only where the vessels were already brittle, as is often the case in the brain; or after very sudden removal of external pressure (operation for hydrocele, ascites), or in operations for cataract (hæmorrhage into the retina, even with its detachment) ; or in very quickly appearing collateral hyperæmia, as in the opposite side of the brain, after ligation of the common carotid; or in more frequent return of hyperæmia, and, when the tissues are tender, as bleeding from the nose in childhood, bleedings of the air-passages and lungs in youth, cerebral hæmorrhage in more advanced age.

According to more recent experience, very small bleedings from the uninjured walls of vessels occur in every hyperæmia even of short duration. But also somewhat greater capillary bleedings take place, probably very often in hyperæmic parts, but for the most part present no symptoms, because the blood exuded is carried away as soon as it reaches the origin of the lymphatics.

PAIN in active hyperæmia is often wanting ; or it is only dull, or a sense of tightness or of heat ; it is rarely severe, as, *e.g.*, in carious teeth.

FUNCTIONAL DISTURBANCES in congestions are of various importance. Function is sometimes slightly more active, sometimes enfeebled. In CONGESTIONS OF THE BRAIN there arise phenomena sometimes of irritation, sometimes of pressure, sometimes of both at the same time, sometimes only of the former, sometimes only of the latter. These phenomena belong to the psychical, sensory, and motor spheres in various degrees and proportions. Most often there exist symptoms of increased irritability (photophobia, irritability on account of noises), flashes of light, humming in the ears, formication; besides, a feeling of unrest, change of disposition, giddi-

ness, hallucinations and illusions, even delirium, sometimes convulsions; sometimes attacks of mania, etc. Every increase of blood-pressure in the brain causes excitation of the *nervi vagi*, and hence reduction of the pulse. The symptoms of CONGESTION OF THE SPINAL CORD are still little known: this is in part the condition in spinal irritation. In active hyperæmia the SKIN is affected with sensations of heat, prickling, itching, and an imperfect sense of touch. Congestive HYPERÆMIÆ OF THE LUNGS of moderate degree present no symptoms; they are followed by a lively interchange of gases. High degrees cause diminished size of the alveolæ, short-ness of breath, fulness or constriction of the chest, asthma, sometimes short cough; expectoration of frothy sputa streaked with blood is seldom present. In the highest grades, which sometimes appear as an acute affec-tion (without demonstrable cause, or after closure of the pulmonary arteries; apoplexy of the lung), are strong constriction of the chest, even danger of suffocation, great dyspnœa, frothy sputa or the same mixed with blood, etc.,—finally the symptoms of acute pulmonary œdema.

According to TH. WEBER (*Ber. d. Naturf - Vers.*, 1872, p. 159) many forms of nervous asthma, so-called, are dependent upon a hyperæmia of the bronchial mucous membrane, in consequence of nervous influence. I have seen an old man who had been many years sexually continent as a widower, and who, having married again, experienced the severest pulmonary congestions (great dyspnœa, cough, bloody and serous expectoration) at each attempt at coition.

The SECRETIONS become changed in many ways by congestive hyperæmia. They mostly become more abundant, either from the beginning or after a short duration of the hyperæmia: thus that of the skin, mucous mem-branes, kidneys, salivary glands, lachrymal glands; the secretion of wounds. The qualitative changes of the secretions are still little known: in general they appear thinner, as the milk during emotional activity; the urine becomes more abundant and watery, often also albuminous.

Increased sweating in consequence of collateral hyperæmia is also not infre-quently seen in the neighborhood of the larger cicatrices (after deep burns, confluent small-pox).
In the skin, the arterial blood-current divides into three streams occupying three planes : one for the adipose tissue, one for the sweat-glands, and one for the papillæ. The veins, in many places forming a sort of net-work in the upper cuticular layer, are the beginning of the collective veins, which convey the venous blood of all three blood-streams to the subcutaneous veins. (Secondary vascular loops from the papil-lary stream supply the muscular apparatus, the excretory ducts of the sweat-glands and the nerves.) Under certain conditions one or another of these blood-courses may become closed. If, *e.g.*, the skin of the palm of the hand becomes cooled, its papillary layer filled with blood, and there exists an abundant and continuous secre-tion of sweat, there is a contraction of the arteries supplying the papillary stream above both of the deeper vascular layers of the skin, while the blood-streams for the sweat-glands and fat are not affected. The blood present in the venous net-work of the papillary layer acts like that of a dead branch of the other blood-streams in the skin. While the force of the papillary blood-current sinks from contraction of the arteries, that of the sweat-glands and adipose tissue remains undisturbed; the lateral pressure in the upper collective veins of the skin is somewhat increased, the papillary net-work cannot empty its contents into veins, its blood is perhaps dammed back. (TOMSA, *Arch. f. Dermat. u. Syph.*, 1873, V., p. 1.)
Albuminuria in granular kidney, where numerous blood-vessels are obliterated, is explained by the fact, that animal membranes, which under moderate pressure are impermeable to albumen, allow small quantities to pass through during an increase of pressure (collateral hyperæmia). (BARTELS.)
KNOLL (ECKHARDT's *Beitr.*, 1871) found that after section of the splanchnics the secretion of urine increased considerably on the operated side, while upon the other

side it remained unchanged. The light-colored urine, in the first case, showed only a slight diminution in the per-cent. of solid ingredients and urea. The appearance of albumen, as well as the frequent occurrence of an alkaline reaction, is not connected with section of the splanchnic nerve.

Especially interesting in many NEURALGIÆ are the objectively-shown hyperæmiæ and disorders of secretion: in neuralgia of the first branch of the trigeminus there occur redness of the conjunctiva and increased lachrymation; in neuralgia of the second branch, sometimes watery or mucous secretion from the nasal mucous membrane; in that of the third branch, frequent salivation.

DISTURBANCES OF NUTRITION appear only after a longer duration, or more frequent return of hyperæmia: the vessels remain dilated, their walls gradually thicken relatively to their lumen. By these means there arise not only permanent changes in the circulation, which with respect to the existence of the collateral circulation are of great importance; but also permanent nutritive disturbances, which are shown sometimes in physiological hypertrophy (in muscles, bones), sometimes are of a pathological nature, as hypertrophies of the skin, bones, glands, thickening of the arteries and continued disturbance of function, as, *e.g.*, in the brain of the intemperate. As soon as true nutritive changes appear in hyperæmic parts, active hyperæmia passes into atrophy, hypertrophy, or inflammation.

A large number of experimental sections of vaso-motor nerves have shown, that nutritive disturbances in hyperæmic parts appear more easily and quickly in young than in older animals; that they are sudden and severe inversely as the hyperæmic part is protected from external injurious influences (SCHIFF, SNELLEN, MEISSNER, and others). Correspondingly, great nutritive disturbances in man are proportionately lighter, if the sensory and motor nerves are paralyzed at the same time with the vaso-motor nerves; as especially in severe diseases of the spinal cord and brain. See also the interesting case observed by the author, in HÄNEL, *Z. Casuist. d. vasomot. Neur.*, Leipz. Dis., 1868, p. 10.

Collateral hyperæmia in the vicinity of new-formations and the consequently increased supply of nutritive material, probably in part cause their quicker growth.

GENERAL SYMPTOMS in consequence of hyperæmia occur only when the latter is very extensive: *e.g.*, in the heat of fever, when it affects the whole skin, either in burning of the surface, or in paralysis of the splanchnics, when it affects most of the abdominal organs. The general symptoms have then their origin partly in anæmia of other important organs, especially of the brain and lungs; partly in changes in the circulation (decrease of blood-pressure, retardation of the pulse), respiration (dyspnœa), temperature (decrease), etc.

Physiologically, the general consequences of section of the *n. splanchnici* and of the upper part of the spinal cord are accurately known. After SECTION of the former beneath the diaphragm there follows a DETERMINATION OF BLOOD INTO THE ABDOMINAL VESSELS, the BLOOD-PRESSURE IS LOWERED, THE PULSE BECOMES QUICKER AND SMALLER (in consequence of anæmia of the brain, especially of diminished tonus of the roots of the vagi). The small and quick pulse in many cases of acute general peritonitis is probably thus explained. After section of the upper part of the spinal cord there follows general dilatation of the vessels and decrease of blood-pressure; at the same time there is a lessened frequency of the pulse (LUDWIG).

After extensive burns of the surface, there follows dilatation of the superficial vessels with consequent abnormal supply of blood and elevated temperature, on the one hand; on the other hand, the dilatation of the vessels causes a diminution of the blood-pressure, and finally paralysis of the heart. Both explain the manner of death from great burns, better than the earlier assumption of nervous collapse, etc. (FALK, *Virch. Arch.*, 1871, LIII., p. 27.)

According to HEIDENHAIN, an increase in the pressure of the aortic system and a diminution of temperature in the interior of the body appear through irritation of

a sensory nerve or through direct irritation of the med. oblongata : the latter effect is dependent upon an increased temperature of the surface. See also LOVÉN (p. 160).

In later years, a few special, more or less obscure diseases have been proposed as consequences of a diminished function of the sympathetic : Basedow's disease* (TROUSSEAU, REMAK, RECKLINGHAUSEN, GRAEFE, GEIGEL), diabetes (SCHIFF, ETC.), intermittent ophthalmia (EDMONSTONE, ETC. ; EULENBERG-LANDOIS). — According to RISEL (*D. Arch. f. klin. Med.*, 1870, I., p. 34), the cœliac plexus and semi-lunar ganglia, nerves lying in the neighborhood of the cœliac artery, are affected in *morbus Addisonii.* In consequence of this, the vaso-motor nerves are paralyzed, the abdominal vessels are overfilled with blood, while all other vessels are deprived of it.

B. PASSIVE OR MECHANICAL HYPERÆMIA. STAGNATION OF BLOOD.

(Infarction. Venous hyperæmia.)

PASSIVE HYPERÆMIA consists in an increased quantity of blood in a part, less often through primary decrease of the general blood-pressure, usually through increase of the resistances to be overcome (hindrances to the flow of blood out of the veins), or through both causes at the same time. The blood then stagnates more or less in the venous radicles, if the hindrance is not quickly removed again, or if the blood does not find a lateral channel. The latter is never entirely the case, and thus there results a RETARDA-TION OF THE CIRCULATION within the hyperæmic region (opposed to active hyperæmia, where the blood current is usually accelerated). This is further promoted through the greater extent of the venous system in proportion to that of the arterial.

THE CAUSES OF PASSIVE HYPERÆMIA are :

1. DECREASE IN THE HEART'S ENERGY (mostly from albuminous or fatty metamorphosis of the heart), as it occurs in severe acute diseases, in fevers of long duration (hectic, typhous, pyæmic, etc., fever), or, without fever, in marasmus of different kinds, without increase of local resistances. The consequences of decrease in the heart's energy appear in those places chiefly which are farthest from the heart (hands, feet, ears), or in those in which one of the following causes is added.

O. WEBER (l. c., p. 55) designates as ISCHÆMIC HYPERÆMIA those arrests of the blood in the veins AFTER CLOSURE OF THE ARTERIES SUPPLYING THEM, especially in incomplete collateral circulation. In the affected capillaries and veins the pressure ceases altogether with the closure of the arteries, or is considerably diminished. The veins are over-filled with blood, and with the capillaries are widely distended : there result exudations of the serum of the blood through the walls, hæmorrhages, etc.

2. DIMINUTION OR ENTIRE LOSS OF THE TONUS OF THE VEINS (see p. 163–4) is sometimes found after the operation of extreme cold or heat, as a conse-quence of severe inflammations of the walls of the veins or of their sur-rounding tissues, probably also through disturbances connected with the influence of the nerves.

According to FALK (*Virch. Arch.*, 1871, LIII., p. 27), the dilatation of the vessels of the skin, which appears in consequence of extensive burns, is not congestive in character, but a result of diminished elasticity of the walls of the vessels and of the surrounding tissues.

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* This should be called GRAVES' DISEASE by right of priority.—[ED.]

3. INCREASE OF LOCAL RESISTANCES. Such exist, first of all, in the chronic form of arteritis, which, through its effect on the inner coat, increases the friction of the blood passing over it, and through those on the middle layer, diminished elasticity and contractility of the vessel. Many hyperæmiæ and hæmorrhages in inflamed parts, in tumors and their vicinity, depend upon this.

The natural effect of the difficulty is chiefly on the veins. It appears as soon as the muscles become relaxed, or are only partially active. In men who stand long (type-setters, bakers), or who are sedentary (students), or who lie for a long time (men with fractures of the lower extremities, sick of all kinds), it leads to dilatation of the veins and, especially in cases of the last-mentioned kind, to HYPOSTASES. These are met with chiefly in the skin of the back and hips, heels, trochanters; in the scrotum; in the posterior and lower parts of the lungs; sometimes also in the back part of the brain and spinal cord, bladder, prostate, uterus; in the posterior surface of the kidneys; in the deeply lying portions of the intestines. These hypostases occur on both sides from continuous lying on the back; in the corresponding side, in protracted lying on one side. Hypostasis of the lungs is promoted by the weakness of the respiratory muscles, want of force in the heart's contractions, atony of the vascular coats, perhaps also by blood-changes.

Members, especially the fingers, which are stiff in their joints after old inflammations, are often colored bluish-red, and are subjectively and objectively colder.

CHOKING—CONGESTIONS IN THE STRICTER SENSE, HYPERÆMIÆ OF COMPRESSION, arise where a direct obstruction renders difficult the flow of venous blood and a sufficient collateral circulation is not present. Here belongs COMPRESSION OF THE VEINS, e.g. of those of the pelvis and lower extremities by the pregnant uterus; the accumulation of fecal masses against the hæmorrhoidal veins; the action of all constricting articles of clothing, especially in women and soldiers; the action of trusses, of bands of all kinds, of tumors in the extremities; in narrow cavities, that of exudations; the consequences of contractions of cicatrices, as well externally in the skin as in the glands, as, e.g., in granular liver, in the kidneys; of strangulation in ovarian tumors; those of the intestinal veins in strangulated hernia, of the rectal veins in piles, etc. Farther, the formation of COAGULATIONS AND CONCRETIONS IN THE VEINS; the manifold and varicose enlargement of the veins in the lower extremities, in the seminal cord, in the pelvis; in and around the uterus; ulceration of the veins; cavernous dilatation of the vessels.

Contraction of the veins probably also occurs in an independent manner; at any rate, we know nothing to the contrary. Experimental examinations of intestinal pressure were made by SCHWENINGER (*Arch. d. Heilk.*, 1873, XIV., p. 300).

Some DISEASES OF THE LIVER, of the connective-tissue and remaining elements of the fissures of the liver, of the trunk of the portal vein, are followed by venous hyperæmia of the radicles of this vein; but which may, in part, be compensated for by means of anastomoses of the portal vein with other veins.

Many DISEASES OF THE HEART, especially those in which the blood accumulates in the left ventricle (insufficiency of the mitral valve and stenosis of the left auriculo-ventricular opening, etc.), and those of the LUNGS, in which either the aspiration of venous blood is lessened, or its passage

through the pulmonary vessels is obstructed, likewise belong to this class, although thereby there finally appears hyperæmia of the whole venous system. In the cardiac diseases mentioned above, first of all, the flow of blood out of the pulmonary veins is obstructed; farther on the arrest is continued through the pulmonal veins, partly into the bronchial veins (hence chronic bronchitis), partly through the capillaries into the pulmonary artery, the right side of the heart, to the liver and through the capillary system of the latter into the abdominal cavity (abdominal hyperæmia).

According to J. C. LEHMANN (*Untersuchungen des Blutdruckes bei Brustkrankheiten: Bibl. for Laeger*, July, 1869, p. 1), the changes peculiar to blood-arrest (hypertrophy and dilatation of the right side of the heart, cyanosis of the liver and kidneys, nutmeg-liver, hyperæmic distension of the spleen, cyanotic coloring of the skin, and dropsy) occur oftenest and are most marked in chronic bronchitis, while in pulmonary phthisis and empyema they are observed most rarely. This does not depend alone on the fact that the mechanical obstruction to the pulmonary circulation is greater in chronic bronchitis, but upon the aggregate quantity of blood in the body and in the whole duration of the disease: the greater the first and the longer the last, so much the sooner, *cet. par.*, can congestions appear. Both these last causes are, in chronic bronchitis, directly favorable to the development of a congestion, as they cause no, or no considerable, emaciation and anæmia, and usually last a very long time; while phthisis is accompanied by great emaciation and anæmia, and is of shorter duration.

An especial DISPOSITION to venous hyperæmia is found in certain parts of the body: in the hæmorrhoidal veins, whose walls have no valves, and whose blood has to pass through a second capillary system; in the left spermatic vein, since it opens into the left renal vein (frequent cause of varicocele on the left side), etc. This disposition is sometimes acquired, *e.g.* in the region of the saphenous vein, from pregnancy, etc.; sometimes hereditary, *e.g.* in the hæmorrhoidal veins.

The SYMPTOMS OF PASSIVE HYPERÆMIA are generally more lasting as those of congestion, since their causes are mostly continuous. They also, for the most part, appear more slowly than in the latter, and in many cases never again disappear. They finally affect all the larger divisions of the body, since the causes, for the most part, act widely, and since all veins freely anastomose with one another.

A DARK BLUISH-RED COLOR of the part (an extremity, the lips and mouth, etc.) is the most striking symptom. This coloring is in consequence of the dilatation of the veins and capillaries, of the greater accumulation of the blood-corpuscles, of the retarded circulation, and of the resulting increased taking-up of carbonic acid out of the tissues.

COHNHEIM (*Virch. Arch.*, XLI., p. 220), in microscopical observation of the web of a frog after ligation of the crural veins, saw the arteries and veins dilate only a little, the capillaries hardly more than about a fifth of their original diameter. However, after longer duration of congestion, there appears, as may be demonstrated in the visible parts of man and in the dead, a considerable dilatation. In the liver, *e.g.*, this may become so considerable that the hepatic cells altogether disappear, or are in various ways compressed.

COHNHEIM saw the blood-movement a few seconds after ligation of the crural veins, become pulsating and rhythmical: by the sudden closure of the veins the resistance in the veins and capillaries so increased, that it was overcome only by the systole.

COHNHEIM farther observed, that after ligation all the vessels become densely filled with blood-corpuscles. In the arteries and veins the character of the stream disappears, the blood-corpuscles come into immediate contact with the inner contour of the vessel's wall, the red and white globules in confusion. This is still more striking in the capillaries: the quantity of blood-globules becomes greater with every systole; they lie at first with their long axis in the direction of the stream, but soon their

surfaces are opposed to the stream. Their contours are still visible. After some time, twenty minutes, the capillaries appear filled with an altogether homogeneous red substance, in which only the colorless blood-globules are still visible. After a short time this color becomes bluish-red. The movement is at the same time completely arrested.

The behavior of the LYMPHATICS in congestive hyperæmia is still almost unknown. In the lower grades of it, they are, according to many (GOLGI, etc.), considerably dilated; in higher grades and later stages, especially if the parts are dropsical, this is certainly the case. (*Vide infra.*)

When congestive hyperæmia extends to parts of the skin and to the finest veins, whereby the skin, and especially the prominent parts (nose, lips, cheeks, fingers), mostly also the visible mucous membranes, become bluish colored, these parts are called CYANOTIC.

In a narrower sense, by general CYANOSIS, blue disease, is understood the quickly or slowly appearing state, in which there arises a uniform coloration of the whole skin and mucous membranes through a restriction to the interchange of gas in the lungs, and through a retardation of the blood-stream in the capillaries and veins.

A LOWER TEMPERATURE in passively hyperæmic parts proceeds, in part from the slower current of blood, in part from the inconsiderable transformation of material. It is most striking in the peripheric parts subject to greater cooling off, and is perceptible as well to the patient as to the physician.

If the stagnation of blood takes place quickly, the temperature of the part is at first increased by means of the arterial supply : O. WEBER found after ligation of the veins in the ear of a rabbit, a rise of from 2 –3° C.

Large HÆMORRHAGES upon free surfaces, or into the parenchyma, usually occur only from free and delicate vessels (inner meningeal layers of the brain, alveoli of the lungs), or from diseased vessels, or in congestive hyperæmia of high degree. (*Vide* HÆMORRHAGE.)

According to COHNHEIM, there appear in the web of a frog, at the earliest forty-five minutes after ligation of the femoral vein, at the periphery of the capillaries, regularly dilated and filled with a uniform red substance (the confluent red-globules), small rounded knots of the same color, which swell out more and more, present rounded excrescences, and finally become large, irregular, uneven masses. These then fall apart and appear to be composed of red-globules, which now lie outside of the vessel. This transmigration of blood-corpuscles takes place also in some of the smallest veins, when the aggregation of blood is especially great. It is doubtful, that the colorless corpuscles also pass through. According to BASTIAN (*Brit. Med. J.*, 1868, p. 425), red globules, as well as white, leave the vessels in venous stases, scorbutus, etc., by means of amœboid movements.

VIRCHOW (*Beitr. z. Gebrtsch.*, 1872, I., p. 323) has seen chronic hyperæmia exist with rust-colored sputa, and later in the dead body true brown induration of the lungs in chlorotic women without valvular disease.

Bleedings, *e.g.*, into the rectum, from the nose, act favorably on passive hyperæmiæ, as well by the local as by the general decrease of the blood-mass. They may on this account also be resorted to as therapeutic measures, as for example in congestion of the vessels of the head.

The FUNCTION of parts is diminished partly on account of the retardation of the circulation and of the little amount of tissue transformations, partly on account of the pressure which the dilated capillaries exercise upon the surrounding parts (brain, glandular cells), partly on account of the displacement of other substances, *e.g.*, of the air in the pulmonary vesicles. In the BRAIN there are presented signs of depression of the psychical, motor,

and sensory functions, dulness, vertigo, affections of the senses. In the
NERVES of the extremities there is a feeling of numbness and weakness.
The number of HEART-BEATS is usually lessened. The vaso-motor nerve
centres become irritated; small arteries contract, blood-pressure rises. The
pupils are mostly dilated. In the MUSCLES there appears a diminished
capacity for motion, as well in those of the extremities, as in the heart;
also for the most part in smooth muscular fibres (e.g., in impaction of the
intestines). In the RESPIRATORY ORGANS also it gives rise to slight or no
bronchitis and dyspnœa, which sometimes in a chronic manner becomes
most severe. The GLANDULAR ORGANS, in which velocity of the blood-
stream and rapidity of excretion stand in direct proportion one to the
other, secrete less, the quantity of urine becomes reduced, the urine more
concentrated, of high specific gravity, albuminous; the sediment, for the
most part very abundant, contains urates, casts, etc.

If we breathe in as deeply as possible, and then with the glottis closed, by means of
the muscles of expiration as well as by compression of the thorax by the arms, the
greatest possible pressure is exercised upon the lungs, the heart's impulse and tone
and pulse gradually become weakened, and may entirely disappear; the cervical and
facial veins become swollen, the skin and mucous membranes of the head become
bluish-red, followed by dizziness and even fainting (ED. WEBER, DONDERS).

According to LANDOIS (Med. Centralbl., 1867, No. 10), hyperæmic states, especially
venous stasis of the medulla oblongata, can give rise to ATTACKS OF EPILEPTIFORM
CONVULSIONS. HERMANN and ESCHER (Arch. d. ges. Physiol., 1870, III., 1 H., p. 3)
have likewise shown by experimentation on cats, that the same convulsions occur in
diminished as well as in increased supply of blood to the brain. Hence, the imme-
diate cause of both forms of convulsions is the same, namely, a want of oxygen,
and the accumulation of carbonic acid in certain regions of the brain. Accord-
ing to NOTHNAGEL (VOLKMANN'S Samml. Klin. Vortr., 1872, No. 39), the symptoms
at the beginning of an epileptic attack (coma and general convulsions) have their ori-
gin in arterial anæmia of the brain, particularly of the pons, and medulla oblongata;
while those appearing late in the attack (coma, general convulsions, high degree of
venous hyperæmia of the face) proceed from venous hyperæmia. The same irritant,
which acts upon the centre of respiration in the spinal cord, incites to increased
activity all neighboring centres concerned in an epileptic attack, the automatic centres
so-called: the vaso-motor centre, the centre for convulsions, the nuclei of the cere-
bral motor nerves.

Whilst most functions are diminished by venous hyperæmia, a motion appears in
smooth muscular fibres. According to MEYER and BASCH (Oestr. Jahrb., 1871, p.
142), stases of blood in the intestinal canal excite its muscular fibres to motion:
"dyspnœa of the intestines causes their contraction." In the same manner conges-
tive hyperæmia is the cause of movements in the uterus (OSER and SCHLESINGER, vide
p. 169).

WATERY TRANSUDATIONS arise very easily in parts which have long been
subject to venous hyperæmia. They appear in organs of large superficial
extent (skin, etc.), and in serous cavities, as dropsy. In the mucous mem-
branes there appear CHRONIC CATARRHS, as most often affect those of the
respiratory passages and digestive tract; here the anomalies of secretion
are still very obscure.

A moderate SWELLING of the part is frequent in venous hyperæmia. In
external parts this is easily demonstrated, in internal parts only in the
liver (especially in insufficiency of the mitral valve). It is sometimes pain-
less, sometimes connected with a sense of weight, or with a dull pain, a
feeling of tightness or of pressure.

Passive hyperæmia of very long duration may be followed by HYPER-
TROPHY of the dilated vessels and of the tissues themselves: the former,
most often in the leg in varices, also in the anus; the latter in the con-
nective tissue of the skin, mucous membranes, glands (cyanotic induration

of the kidneys, etc.).   More frequently congestive hyperæmia gives rise to
ATROPHY, *e.g.*, red atrophy of the liver; not infrequently, however, the
diminution of the part is concealed by the serous swelling.   GANGRENE
(*decubitus*) arises mostly only from external pressure (in the region of the
hips, etc.), or in total arrest of the circulation.

GENERAL SYMPTOMS seldom appear in congestive hyperæmia of single
parts of the body, but very early in consequence of general anæmia, and of
the lowering of the blood-pressure, which, *e.g.*, is present in over-filling of
the portal vein and its roots (experimentally—in convulsive states ? in
pressure, etc., upon this vessel), or after burns of the skin of large extent,
producing dilated vessels.

BODDAERT (*Extr. du bull. de la soc. de méd. de Gand.*, 1872), by ligation in rabbits
and guinea-pigs of both external and internal jugular veins, and simultaneous section
of both cervical sympathetics, produced a not inconsiderable exophthalmos, which
existed many days, and again gradually disappeared, with the establishment of the
collateral circulation. B. ligated also the inferior thyroid veins, followed by swelling
of the thyroid gland. B. holds the great acceleration of the heart's contractions,
from paralysis of the cervical sympathetic, to be the primary condition of BASEDOW's
DISEASE, through which contractions a sufficient emptying of the veins during dias-
tole is prevented and a venous congestion is produced.

When the causes of venous congestion quickly disappear, there appears
in a short time a RE-ESTABLISHMENT of the normal conditions.   This may,
however, also take place if the congestion remain longer; the circulation
again becomes free, first of all in the veins, then in the capillaries; the
exuded serum disappears from the tissues through the lymphatics, the red
blood-globules partly degenerate into fat, partly enter upon a pigmentary
metamorphosis.

COHNHEIM, in his experiments, saw, after restoring the current of the blood by re
moval of its obstructions, the homogeneous red masses (confluent red-corpuscles)
sometimes in a few minutes again separate into their individual normal elements.
The red-globules found confined in the vessels' walls in their passage through them,
partly passed on to the exterior, while others were broken off by the blood-stream, and
are carried onward. All were gone in from twelve to sixteen hours after loosening
of the ligature.
According to GUYON (*Arch. d. Phys.*, 1868, I., p. 56), the pulse in the carotid can-
not be felt during strong muscular efforts, as in parturition, while that of the radial
continues. G. explains this by a swelling of the thyroid gland (from venous conges-
tion) and a simultaneous contraction of the muscles of the neck, so that the carotids
are compressed by them. In this manner venous congestions in the head and brain,
threatening danger, may be checked by a kind of self-controlling of the arterial
supply.

3. THROMBOSIS AND EMBOLISM.

The older researches of WEPFER (1658), GOHL (1710), etc. J. HUNTER, *Tr. of a
Soc. for the Impr. of Med and Chir. Knowl.*, 1793.—HODGSON, *Von d. Krankh. d.
Artt. u. Venen.* Transl. by KOBERWEIN, 1817.—ALIBERT, *Rech. sur une occlusion
peu connue des vaisseaux artériels considérée comme cause de gangrène*, 1828.—FRANÇOIS,
Ess. sur la gangrene spontanée, 1829.—STILLING, *Die Bildung u. Metamorph. des
Blutpfropfes u. s. w.*, 1834.—STANNIUS, *Ueb. d. krankh. Verschliess. grösserer Ven-
enstämme*, 1839.—GULLIVER, *Med.-Chir. Transact.*, 1839.—ZWICKY, *Die Metamorph.
des Thrombus*, 1841.—TIEDEMANN, *Von d. Vereng. u. Schliess. der Pulsadern in
Krankh.*, 1843.—PAGET, *Lond. Med. Gaz.*, 1844.—PORTA, *Delle alterac. patol. delle
art. per la legat. e la tors.*, 1845.—HASSE, *Ztschr. f. rat. Med.*, 1846, p. 91.—VIRCHOW,
Ztschr. f. rat. Med., 1846, V. ; *Fror.'s Not.*, 1846 ; *Traube's Beitr.*, 1846, II., p. 1 ;
Arch., 1847, I., p. 272, V., p. 275, IX., p. 307, X., p. 179; *Ges. Abhandl.*, pp. 57 u.
219; *Hdb. d. Path. u. Ther.*, I., p. 156.—MEINEL, *Arch. f. phys. Heilk.*, 1848.—BEN-

NET, *Monthly Journ.*, 1850. —SENH. KIRKES. *Med.-Chir. Transact.*, 1852. —RÜHLE, *Virch. Arch.*, 1853. V., p. 189. —TUFFNELL, *Dubl. Quart. Journ.*, 1853. —KLINGER, *Arch. f. phys. Heilk.*, 1855. —COHN, *De embolia ejusque sequelis*, 1856 ; *Klinik der embolischen Gefässkrankheiten*, 1860. —DUSCH, *Ztschr. f. rat. Med.*, C. VII. —PANUM, *Günsburg's Ztschr.*, 1856, VII. ; *Virch. Arch.*, XXV., pp. 308 and 433. —BECKMANN, *Virch. Arch.*, 1857, XII., p. 59. —SCHÜTZENBERGER. *Gaz. méd. de Strasbourg*, 1857. —FROMMANN, *Virch. Arch.*, 1859, XVII., p. 135. —GRAEFE, *Allg. Wien. med. Ztg.*, 1859, No. 14. —O. WEBER, *Hlb. d. Chir.*, 1865, I., p. 69. —VOLKMANN, *Langenbeck's Arch.*, 1866, V., p. 330. —THIERSCH, *In Pitha-Billroth's Hlb. d. Chir.*, 1867, I., 2. Abth., 2. H., p. 531. —COHNHEIM, *Unters. üb. d. embol. Proc.*, 1872. (Consult also the literature of PYÆMIA.)

From various local and general causes there occurs DURING LIFE, within the vessels, a COAGULATION OF THEIR CONTENTS. The coagulum is distinguished from that arising during the agony, or immediately after death, by the term THROMBUS. Such a coagulation once having taken place, *e.g.* in the veins, the whole channel may become obstructed, and the process continue peripherically into the smallest branches ; it proceeds toward the centre as far as the nearest larger inosculating branches ; the coagulum projects somewhat from the mouth of the vein, and since the blood-stream of the other vein comes in forcible contact with it, here arises a thrombus which may again extend backward into the distribution of the second vein.

But it not infrequently happens that the blood-stream coursing along the free unobstructed vessel, comes in contact with the projecting part of the coagulum, and carries a piece away along with it. This may also occur in a coagulum which does not completely obstruct the vessel. These free coagula or pieces, if they belong to the veins of the systemic circulation which do not open into the portal vein, must pass the right side of the heart ; from here they go into the lungs, and are, according to their volume, driven into a larger or smaller branch of the pulmonary artery. If they have their origin in the roots of the portal vein, they are carried away by that vein, and stick fast in its hepatic branches, etc. This occurrence of obstructing vessels by coagula which have been transported from other parts, is called EMBOLIC THROMBOSIS, or EMBOLISM. The obstructing plug itself is called EMBOLUS.

The thrombus and the embolus are, in the greater proportion of cases, coagula of blood ; both may be formed of other substances. The consequence, however, is then almost always a coagulation of the blood, for the most part around the primary thrombus or embolus.

A. THROMBOSIS.

THROMBOSIS, *i.e.* THE COAGULATION OF THE BLOOD WITHIN LIVING VESSELS, follows the same laws as coagulation outside of them. (*Vide* p. 155.)

Thrombosis occurs frequently in the heart, in the arteries and in the veins of medium size, seldom in the capillaries, oftener again in the lymphatics.

AN AUTOCHTHONOUS or PRIMITIVE THROMBUS is one which remains confined in the part in which it first arose, especially in the heart, also in the vessels. It lies in contact either with the inner surface of the vessel by a greatly varying extent of surface, without sensibly contracting the vessel's channel. Or, it projects farther into the channel, so as to effect a real narrowing of the vessel : so-called PARTIALLY OBSTRUCTING THROMBUS. Or, finally, the vessel's channel, to a varying length, is completely closed by the coagulum : so-called TOTALLY OBSTRUCTING THROMBUS. The shape of this thrombus

corresponds exactly with that of the vessel: if the latter is large and pouch-shaped, the former will be globular; if branched, the thrombus likewise will be branched; but its central part, *i.e.* the end directed toward the heart, always takes the shape of a rounded cone, in the arteries as well as in the veins.

A PROGRESSIVE THROMBUS is one which grows continuously through a various extent of the vessel, which, from small beginnings seldom proceeds quickly, but for the most part slowly and by strata. In the arteries the progress is oftener from the trunks and larger branches toward the smaller branches, while in the veins the contrary usually occurs. Its extension takes place in different ways, first of all, always into the next larger collateral branches.

Exceptions occur in the veins on account of the easy compressibility of their walls. Thus, in obstruction of the right iliac vein, a very long plug is usually formed in the vena cava, while on the left side this rarely occurs, because here the right iliac artery, crossing the left iliac vein, favors the closure of its orifice.

Most of those thrombi are called SECONDARY which arise after primary inflammation of the vessels or of the tissues immediately surrounding them. Many thus designate those also which are continuous from a vessel into one of another kind, *e.g.* from capillaries into veins or into arteries, from veins into arteries, etc.

The coagulum is contiguous with most of the circumference of the vessel. Less frequently there are found between it and the wall, spaces, which are filled with fluid blood: the latter comes from the small vessels which enter in or depart from the vessel at this point.

The CHARACTER OF THE THROMBUS varies. Its surface is always smooth and even, if no especial influences have acted upon it. Thrombi ARE or ARE NOT LAMINATED. The latter occurs from sudden coagulation of an arrested mass of blood, *e.g.* in ligation of vessels; red and white blood-globules are uniformly distributed through it. Laminated thrombi arise during a slow and continuous coagulation with an intermitting force of condensation; they show in transverse section colorless corpuscles in large quantity, and alternate layers of red and white blood-globules. The layers are not perfectly concentric, but are arranged in longitudinal and transverse section, like those of an onion, if the thrombus is situated in a broad cavity (heart, varix), and the latter is attached to a small point; or they are like those of the preceding only in cross section, in longitudinal section consisting of overlying ellipsoidal layers, if the thrombus belongs in a narrow vessel. At first the thrombus is dark- or grayish-red, elastic, soft, moist, and has a smooth, glistening, moist surface of section. Gradually it becomes paler, drier, less elastic, even crumbling; its surface on section becomes dull and lustreless, and is at different points colored red, brown, gray, and yellow. Under the microscope there are to be seen fibrous lamellæ in inconsiderable number, and between them shrivelled white and red blood-corpuscles, chiefly, however, albuminous molecules.

Thrombi are not to be confounded with the coagula found in the dead. As is well known, coagula are found in almost every dead body, in the right side of the heart, when the death-struggle has been prolonged. These are light or dark colored, loose, elastic, soft, and are attached to the valves and cords. The dark coagula consist of fibrin, red and white blood-corpuscles. Frequently the red corpuscles quickly sink, leaving the coagulum formed only of fibrin and colorless corpuscles; it then appears white, or whitish-yellow. These coagula reach from the right side of the heart into a part of the pulmonary artery, but which they never entirely fill; they are continuous

into the venæ cavæ, and thence through all the veins of the body, into which the blood, at the death of the vessels, is driven by the elasticity of the arteries. Coagula are not usually found in the arteries, or only small ones in those of the largest size, similar to those mentioned above.

The fresh, laminated thrombus is distinguished from a simple blood-coagulum : 1, by its laminated structure, which is present in almost all somewhat thicker thrombi ; 2, by its greater quantity of fibrin : hence these thrombi are mostly lighter, firmer, and drier than coagula ; 3, by the greater proportion of white blood-corpuscles over that of the red, which proceeds in part from a retardation of the circulation, in part from the fact that the blood of many affected with thrombus-formation is richer in such corpuscles (those affected by puerperal diseases, and consumptives). The non-laminated thrombus is, in its most recent state, not to be distinguished from a blood-coagulum. Later it is characterized by its metamorphoses.

The FARTHER DESTINY of a THROMBUS varies. Most important are its puriform liquefaction and its organization.

PURIFORM LIQUEFACTION, or SOFTENING, is the usual metamorphosis of laminated thrombi of the heart and veins, in thrombosis of long duration. Then there is found, at first in the middle of the thrombi and extending thence toward the periphery, a liquid at first sharply circumscribed, later more diffuse ; at first more viscous, then of a thin or thick consistency ; which liquid to the naked eye sometimes perfectly resembles pure pus, and sometimes has an ichorous character (reddish or brownish, thin and often of a disagreeable odor). At the beginning there are mixed with it crumbling particles, which are the remains of the more dense fibrinous layers. The microscope then shows, in such thrombi, the elements of true pus only if pus has perforated into the vessel, or if in its wall even there has happened the formation of an abscess. Usually albuminous molecules are chiefly found, later, oil-drops, red and especially white blood-corpuscles, rarely normal, but mostly in a state of metamorphosis.

The ORGANIZATION of thrombus occurs mostly in the non-laminated variety ; less frequently in extensive thrombosis of the veins, with final destruction of the channel of the vessel ; more often in partial thrombosis, in the veins as well as in the arteries, occurring especially after section and ligature. The thrombus filling the vessel (artery or vein) immediately after injury reaches from the wounded point to the nearest collateral branch ; it is accordingly of different lengths, and on one side (or on both) projects into the blood-stream with conical extremities. It is already, very soon after its formation, firmly connected by its base to the inner surface of the vessel, while the remainder lies at first loose in the vessel, and only gradually acquires a firm connection with its internal surface. The coagulum is at first dark black-red, later of a brown color ; in its farther progress it becomes paler, always first in the centre, until after a few weeks or months it assumes a color similar to that of the vessel. In the course of the following weeks, in the thicker coagulation of the following months, it always shrinks more, so that the vessel ends in a conical form, and blind, in cicatricial tissue.

The views held concerning the mode of organization of thrombus are still divided. It certainly does not take place through free exudation ; probably as little through the colorless blood-corpuscles included in it ; perhaps, at least in part, through the colorless corpuscles of the circulating blood, since these pass into the thrombus from the *vasa vasorum*, or through the cells formed outside of the vessel, which cells the vessel takes up. The organization of thrombus takes place most probably, however, through the endothelia of the vessels, as well as through the connective tissue cells of their intima. These grow within a few hours, and are transformed at first into spindle-shaped cells, later into connective tissue and vessels. After seven

or eight days the thrombus, especially at its periphery, is penetrated by a net-work of young capillaries, which in the following days become more and more numerous. In the meanwhile the blood-corpuscles are destroyed, and likewise the fibrin, as in the puriform liquefaction of thrombus. The newly formed vessels of the thrombus and of the intima of the vessel come into communication with the original vessels, and with the newly-formed vessels of the middle coat and adventitia, and thus arises a true circulation through the thrombus. Later, there appears also a communication of the vessels of the thrombus with the channel of the vessel containing the thrombus. The former takes place earliest at the constricted end of ligated vessels, where the cellular coat is drawn over both the inner coats which are curled inward, and when the breach in the centre closed by the coagulum renders immediately possible the inward growth of the vessels of the adventitia. Thus, after four to six weeks, a complete circulation through the thrombus is established, and again gradually retrogrades in the following manner : the vessels again disappear, the primitive jelly-like connective tissue becomes more and more dense, the red blood-corpuscles and fibrinous detritus still present are reabsorbed. Finally, there remains only a small connective tissue plug, poor in vessels, which finally may become so shrunken that it is demonstrable only by the microscope.

The organization of thrombus was demonstrated by the older observations of HUNTER, BLANDIN, LOBSTEIN, STILLING, and ZWICKY, by those more recent of BILLROTH, O. WEBER, THIERSCH, WALDEYER, BUBNOFF, etc.; as well from casual observations in man, as in the course of experiment on arteries and veins. That it does not take place through free exudation was shown by VIRCHOW. O. WEBER (*Berl. klin. Wschr.*, 1864, No. 25) inferred that it was brought about by means of the colorless blood-corpuscles of the thrombus itself.

BUBNOFF (*Med. Ctrlbl.*, 1867, No. 48, and *Virch. Arch.*, XLIV., p. 462), in a number of experiments, found that the contractile cells which are formed outside of the veins take up cinnabar, penetrate the wall of the veins, and by their gradual migration finally come into the interior of the vein itself and reach the centre of the thrombus arising from ligature. From a second series of experiments, in which B. injected cinnabar into the blood from twelve to twenty-four hours after the establishment of a thrombus, it seemed to follow that the cells containing cinnabar within the circulating blood penetrated the thrombus from the *vasa vasorum ;* the white corpuscles belonging to the free circulation thus appeared to be concerned to a slight degree in the organization of the thrombus. From a third series, in which B. injected cinnabar into a thrombus arising from ligature, he concludes, that the colorless blood-corpuscles of the thrombus lose their power of migration, and do not participate in the cell-formation connected with the tissue of organization. B. could not perceive that the epithelium of the veins shared in the organization of thrombus.

THIERSCH, and WALDEYER (*Virch. Arch.*, XL., p. 379) demonstrated, independently of each other, that the endothelium of the vessel played a chief rôle in the organization of thrombus. According to the latter, thrombus is organized through increase of the connective-tissue cells of the vessel-wall and of the endothelial cells of the veins. The intima appears slightly clouded, as if covered with a fine dust. Delicate attachments are then formed, which sometimes are finely papillar, sometimes velvety in appearance. The formation is a perfectly organized, perfectly soft granulation tissue. Consult also TSCHAUSOFF (*Arch. f. klin. Chir.*, 1869, XI., p. 184), and RANVIER (*Nouv. dict de médec. et de chir. prat.*, 1870, XIII., p. 675).

CANALISATION, so-called, of thrombus is probably only a trabecular or net-like organization of it; the canals traversing the thrombus, which arise from partial destruction of the thrombus, sometimes re-establish the circulation through the obturated vein. Especially frequent is this event in the cases of recovery of *phlegmasia alba dolens* in lying-in women.

The fissures which exist in thrombus as permanent passages are always found in the periphery (O. BARTH, *Arch. d. Heilk.*, 1870, XI., p. 63).

CALCAREOUS TRANSFORMATION of a coagulum is rare ; it becomes gradually smaller, firmer, dirty white or yellowish in color ; later, calcareous salts are deposited in it. Thus also are formed the so-called vein-stones.

The origin of PUS, CANCER, and other new formations in thrombus is not yet demonstrated, but from the facts of its organization now known is scarcely doubtful.

A complete RESORPTION of thrombus, with re-establishment of the channel of the vessel, has not as yet been proven, but is probable ; a partial resorption of it is quite frequent.

The BEHAVIOR OF THE WALL OF THE VESSEL at the locality of the thrombus varies. It rarely happens that all macroscopical changes of texture are wanting, unless the coagulum quickly assume the molecular state and the vessel's channel be quickly restored : this occurs usually in venesection. In the organization of thrombus the above-described changes in the wall of the vessel takes place. At other times textural changes are found of a more chronic nature : most often a thickening and greater vascularity of the external coat and surrounding connective tissue, in the veins sometimes also a like degeneration of the middle and inner coats, whereby they assume a more arterial character. In puriform liquefaction of thrombus, the intima becomes clouded, dead and brittle, and after removal of the coagulum is torn away in shreds, or remains firmly attached. Concerning other changes in the endocardium and inner coat especially of the larger arteries, *vide infra*.

THE CAUSES OF THROMBOSIS consist either in stagnation of the blood, or in changes in the wall of the vessel ; or both conditions are present.

1. STAGNATION OF THE BLOOD.

a. CONTRACTION OF THE CHANNEL OF A VESSEL : THROMBOSIS FROM COMPRESSION. Pressure upon vessels causes first a retardation of the blood-current in a part, and coagulation of the blood. The coagulation does not, however, remain confined to this part, but is also continued into the peripheric vessels. Thrombi have their origin thus : by ligature of the arteries or veins ; by suppuration and tumors (tuberculous and carcinomatous lymph-glands), which press upon the arteries and especially the veins ; by effusions of blood from contusions ; by cicatricial contractions ; by dislocation of bones. All these conditions are so much more effective, if the arterial current is weakened. Pressure frequently acts upon the larger vessels not immediately, but rather upon the capillaries of a part or of a whole organ, and affects only the arteries and veins indirectly, since the *vis-a-tergo* of the heart can no longer reach the latter. Coagulation extends then from the capillaries to those larger veins in which the blood-current is normal, less frequently into the arteries. Here belong those coagulations which have their origin in organs organically changed, in the branches of the pulmonary vessels in chronic pneumonia, in the renal veins in parenchymatous nephritis, in the portal vein and hepatic veins in chronic hepatitis ; in part also venous thromboses (traumatic) in wounds of the external surface.

b. SECTION and LACERATION of VESSELS : TRAUMATIC THROMBOSIS. The latter is the most important condition concerned in spontaneous as well as in artificial blood-arrest. If the continuity of a vessel be interrupted,

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there follows either a continuous bleeding, or coagulation of the blood. In the latter case the arteries retract somewhat and become constricted; there arises with or without ligature, a thrombus reaching to the nearest collateral branch, which thrombus for the most part becomes organized.   If an artery be ligated, *e.g.*, in an amputation-stump or (on account of peripheral hæmorrhage) in its continuity, the intima becomes lacerated by the strong tying of the ligature, and is drawn into fine, longitudinal folds which are visible for months, while the middle coat and adventitia are constricted and thereby become plaited.   The folds of the middle coat, and especially those of the intima, contribute very materially to the adhesion of the thrombus.   The VEINS, *e.g.*, in an amputation, become disconnected from the heart, thus being deprived as far as the nearest collateral branch upward of the *vis-a-tergo*, which drives the blood forward.   The latter either settles backward to the wounded surface, because the veins are easily compressed by the surrounding structure; or it coagulates, as always happens, at least to a certain extent.   Moreover, the backward flow is regulated by the position of the valves.   In veins which are without valves, and which from physiological or pathological causes are open (venous plexus of the bladder, rectum, veins of the pregnant uterus, cranial sinuses, cervical veins, veins of bones), thrombosis acquires a much greater extent than in veins which possess valves.   In the latter, the valves exert a very important influence on the extension, etc., of thrombosis.

After every VENESECTION there results a subcutaneous effusion of blood and a coagulum, which extends from the wound in the skin into that of the vein.   This coagulum is sometimes formed already during the venesection (in small wounds of the veins, in shifting of the position of the skin).   The part of the coagulum which protrudes into the vein becomes gradually smaller, denser, and paler, becomes organized, and closes the wound.   Sometimes, however, from, *e.g.*, bad dressings, restlessness, etc., new coagula are deposited on that part of the coagulum which protrudes into the vein; thus, as at first, giving rise to a permanent coagulum, which under certain circumstances is partial, or wholly obstructs the vessel.

In AMPUTATIONS of the extremities the blood found in the lowest part of the veins below the first valve above flows out.   The vein itself usually collapses, partly because its contents have escaped, partly because in veins with very muscular walls (veins of the skin), a true contraction of the latter takes place : the channel then is very small or altogether disappears, the intima is folded longitudinally, the whole wall of the vein is thick.   In like manner, the blood nearest to the surface of the wound usually escapes, if the channel remains open, as in the veins of bones, in indurated hypertrophy of the external coat of veins in soft parts.   Through inflammation affecting the surface of the wound, in which the veins also take part, the channel of the veins becomes narrowed still farther ; the resulting granulations heal into a cicatrix and then permanently close the wound of the veins. Sometimes a small thrombus is formed, if between the wound and nearest valves above there open into the veins one or more smaller branches, from which a little blood flows into their lowest extremity.   At other times coagula are formed of great thickness and length.   These depend upon the relation of the collateral branches which open into the vein above the lowest valves.   If the larger collateral branch open close above the valve, the blood of the cut vein usually remains in the circulation.   But if such a branch is wanting, or is too small, or its other extremity is also cut across, then the *vis-a-tergo* does not affect the blood above the lowest valve. and the blood coagulates usually with a rapidity proportionate with its nearness to the wounded surface.   Besides this natural condition, there are yet others which promote coagulation : unfavorable position of the member, misapplied dressings, weakness of the heart's impulse, blood strongly disposed to coagulation ; ligature of the cut vein (whereby more or less of the blood in the vein to the first valve above escapes at the moment of amputation, but also usually new blood pours into the extremity of the vein through small collateral branches opening into it).   If now a coagulum is formed of more considerable volume, its central end usually reaches to the point where a larger collateral branch opens into the vein. To this free end new coagula are added from the blood of the collateral branch,

whereby the latter even, and from this again the next nearest vein, may become obstructed.

After PARTURITION the uterus presents a large wounded surface (CRUVEILHIER in opposition to W. HUNTER, and others, according to whom a part of the decidua remains behind). Not infrequently, after artificial births, especially after artificial delivery of the placenta, the thick uterine mucous membrane in its superficial as well as its deep layer, is torn off, laying bare the muscular layer. Besides, wounds are frequent in the vaginal mucous membrane, in the external os and within the cervix. In all these wounded parts vessels of various calibre are also lacerated. As soon after parturition as strong contractions of the uterus appear, the uterine vessels also become mechanically compressed, and the blood in them is for the most part driven out. But a part of the blood always remains behind in the vessels, because the contractions are never so strong that the channel of the vessels is completely closed, and, too, because the uterine veins are without valves and the blood flowing off is replaced by new blood. Finally, fine coagula probably always grow from the coagulum found in the uterine cavity into the uterine vessels which open into it.

c. DILATATION OF THE VESSELS AND HEART: DILATATION-THROMBOSIS. With equal quantities of liquid the current is slower directly as the size of the channel; in pouched dilatations of the vessel there are, besides, bordering strata in a state of rest. Since the central part of a stream is normally the swifter, and the peripheral the slower, coagula are mostly from the beginning attached to the wall. They remain either as such and soften, or become organized, etc.; or, the coagulum bordering the vessel-walls gradually forms a complete obstruction to the current. Coagula more rarely from the beginning obstruct the vessel completely: thus in generally dilated veins, *e.g.*, those of the broad ligaments of the uterus. Analogous to this thrombosis of the veins is the formation of coagula in aneurismal arteries, the formation of globular vegetations in the heart, where its walls nearest to the endocardium or throughout the whole extent of their thickness have undergone fatty degeneration or induration.

Here WALDEYER classes those cases, in which, after wounds or operations, gangrene of the part quickly follows inflammatory congestion, and the vessels, especially the veins, after the loss of their contractility and elasticity are speedily transformed into a soft, pliable, pulpy tissue.

d. MARASMIC, ATROPHIC THROMBOSIS exists, when during a reduction of the force of the heart, of the walls of the vessels, of the respiratory muscles and of the muscles external to and in the vicinity of the veins, coagula are formed in the larger veins, especially in the crural and iliac, in the muscular branches (those of the glutei and of the lower extremities), in the venous plexus of the pelvis, in the cranial sinuses, etc. The ease with which this takes place is proportionate to the quietude of the person affected. The first beginnings of coagulation occur in the angle behind the valves. This thrombosis is often found in those who are in a state of low nutrition after severe operations, for whom a long period of quiet lying down, is necessary; it is a frequent sequela of disease, of severe febrile diseases, especially of typhoid fever; it is a common complication of chronic tuberculosis, of chronic affections of the joints and bones, of severe affections of the muscles, of trichinosis.

2. CHANGES AFFECTING THE WALLS OF THE VESSELS.

a. ROUGHNESS OF THE INTERNAL COAT OF THE VESSELS, dependent upon their degeneration (fatty metamorphosis, etc.), or upon infiltration of pus into them, or new-formations (granulation-cells, as in organization of

thrombus — *vide* p. 192), which conditions cause at first a thrombosis lining the vessels, then not infrequently one of a general character. These conditions are found in inflammations of the coat of the veins, especially in abscesses of them, or of the structures surrounding them, in new-formations, especially cancer, which perforate the veins, in chronic endarteritis, and in endocarditis.

In experiments with respect to the relations existing between the intima and the blood in closed venous pouches, DURANTE (*Oestr. Jahrb.*, 1871, p. 321) found that the blood remained liquid so long as no inflammatory changes had taken place through the mechanical irritation of the needles used, and that coagulation of the blood went hand in hand with changes of the endothelium. D. therefore assumed, that the fluidity of the blood shut up in a vessel is dependent upon the normal functions of the vessel's walls.

PHLEBITIS in its various forms is a chief cause of thrombosis in severe wounds of every kind, frequently with purulent or ichorous liquefaction of the thrombus and consecutive pyemia. ENDOCARDITIS chiefly affects the valves, especially the auriculo-ventricular valves. Unevennesses arise on the surfaces; at first loosening or hypertrophy of the endothelium, then thickening and granulations of the surfaces; finally, chalky and fatty metamorphosis of the whole valve. All these inequalities become the causes of numerous deposits from the blood, which in form of warts, condylomata, etc., attach themselves to the valves and firmly adhere to them (vegetations, excrescences, etc.). Chronic ENDARTERITIS, which occurs in arteries of every calibre, causes by fatty degeneration of the endothelium and of the normal or hypertrophied innermost layer, or by calcification or ossification, or softening of the latter, sometimes only superficial unevenness, sometimes deeper losses of substance, which give occasion to coagulations, so much the more, if the middle coat simultaneously degenerate, with loss of its elasticity and contractility, and the vessel is uniformly or irregularly dilated.

b. FOREIGN BODIES in a similar manner give rise to coagulation in the vessels. For example, needles, grains of shot, splinters of bone; or thread, which, often for the sake of experiment, is drawn through the vessel. Coagulation occurs first in the immediate neighborhood of the foreign body. Blood-coagula themselves, thrombi as well as emboli, act in the same manner as foreign bodies.

In this also is included HÆMORRHAGIC thrombosis; in bleedings coagulation of the extravasated blood usually continues through the injury into the vessel. (*Vide* p. 194.)

c. CHEMICAL SUBSTANCES cause coagulation of the blood, when they either effect changes in the blood and wall of the vessel at the same time (caustics), or when they through the latter, without materially changing it, coagulate its contents. In the latter, according to others (*vide* PYÆMIA), the ichor of mortification, and bad pus perhaps also act in a mechanical manner, giving rise then for the most part to an ichorous softening of the thrombus.

Not infrequently thrombosis has its origin in MANY CAUSES at the same time, in arrest of the blood, and changes of the walls of the heart and vessels, often without the first or most important cause being recognized in the living, or in the body after death.

COAGULA OCCURRING IN NORMAL VESSELS continue their growth in a vessel, their origin being either in a branch, or in the vessel itself. In the first case, the point of the coagulum acts as a foreign body, and coagulation may thus extend, *e.g.*, from the veins of the lower part of the thigh into the vena cava, and even to the heart. The blood thereby coagulates mostly also in those veins which end near that first occupied by the thrombus, as well as sometimes in veins of the same name in the other half of the body, if the coagulation once extends to the vena cava, and into all its

branches. The branches of a vein become much more easily obstructed after its thrombosis.

Or, the coagula occurring in normal vessels are secondary. Here belong the coagula in veins the capillaries of which lie in organs infiltrated with pus or cancerous matter ; the coagula in arteries, the periphery of which is obstructed by gangrene or intense suppuration.

Finally, obstructions which appear in arteries after embolism are continued through the capillaries into the veins, and venous thrombi may become the cause of new emboli.

THROMBOSIS OF THE CAPILLARIES has an importance only with respect to its influence upon the healing of wounds, and chiefly through its continuance into the arteries, and especially into the veins.

THROMBOSIS OF THE LYMPHATICS is less frequent than that of the veins, and has been observed only in isolated localities.

The coagulability of normal lymph is very small, in spite of its contained fibrin, and therefore shows little disposition to thrombosis. Under pathological conditions, however, normal lymph is supplanted by another liquid, which is either a transformed fibrinogenous substance, or in part a special fibrino-plastic material exciting coagulation. (A. SCHMIDT.)

A lymphatic thrombosis is found in many severe puerperal fevers. The uterine lymphatics, often over a large extent and far beyond the uterus, are uniformly dilated or knotted, and filled with solid or fluid, yellowish, often puriform masses. Large pouches are oftenest found in the *lig. latum*, especially in the *ala vespertilionis* near the insertion of the tubes, also deeply near the lateral borders of the uterus, even to the attachments of the broad ligaments, and at the other extremity near the *vasa spermatica int-rna*, reaching as far as the lumbar glands ; they are found also in the wall of the uterus, especially of the cervix; also in the ovaries, which from their hilus are sometimes closely interwoven with such obstructed and dilated lymphatics (VIRCHOW, *Arch.*, XXIII., p. 415).

Consult also the observations of BIESIADEZKI (l. e.) and of the author (*Arch. d. Heilk.*, 1870, XI., p. 51). (*Vide* PYÆMIA.)

CONSEQUENCES AND SYMPTOMS OF THROMBOSIS.

These in general consist in narrowing or complete closing of the obstructed canal. They are distinguished from the symptoms of embolism by their comparatively slow appearance. They change not only with the size and metamorphoses of the thrombus, with its relations to the wall of the vessel, with the kind of channel affected (heart, artery, vein, lymphatic), but they also show other and manifold differences, which allow no farther general consideration.

The consequences and symptoms of THROMBOSIS OF THE VEINS depend upon the size of the veins, upon their depth (subcutaneous or deep veins, etc.), upon the thickness and length of the thrombus, the rapidity of its formation, its metamorphoses, upon the duration of the thrombosis, upon the possibility of the formation of a collateral circulation, etc.

Thrombosis of the veins runs it course WITHOUT SYMPTOMS, if the obstruction is incomplete, or if it affects a communicating branch and there are sufficient collateral branches. Thus in the deep veins of the extremities, in the uterine plexus, vesical plexus, etc., where there exist numerous communicating branches. The smaller veins usually remain free, and thus the superficial vessels appearing distended, supplying the collateral circulation.

If thrombosis affect the small veins, and the collateral communication be imperfect, without complete stasis affecting a large territory, then the reaction is confined to the wall of the vessels immediately affected, whose vessels of supply are ob-

structed: there arise a slight inflammatory swelling with moderate redness, slight pain, and watery infiltration of cellular planes; sometimes also a stronger irritation with limited suppuration. This is most often seen in hæmorrhoidal tumors—hæmorrhoidal sweat and excretions, itching at the anus, abscesses in the surrounding tissues, phlegmons in varices (O. WEBER).

According to FRIEDLÄNDER (*Phys.-anat. Unters. üb. d. Uterus*, 1870) the placental portion of the uterine sinuses is in great part obstructed at the eighth month of pregnancy, and, from the accumulation within them of large multinuclear cells, there results coagulation of the blood and organization of the coagulum. The process of shrinking of the latter goes on so slowly, that the thrombi retain their relative size for almost a half-year after child-birth, and on the cut surface of the uterus appear as gelatinous, transparent bodies.

But if large venous trunks, as the crural or iliac, are obstructed, the thrombi fixed, and the collateral circulation insufficient, then there appear symptoms of BLOOD-STASIS, chiefly ŒDEMA. This œdema is usually unilateral, and generally in those sick with dropsy, œdema of the extremities with venous thrombosis is for the most part more marked. Œdemas are usually painless; painful in the highest degree when the obstructed and somewhat dilated veins lie near nerves, as, *e.g.*, the crural close to Poupart's ligament: hence the name *phlegmasia alba dolens* for the œdema, for the most part painful, resulting from obstruction of veins in lying-in women. Serous effusions occur in the region of the capillaries and venous radicles: hence they first appear in distant parts, *e.g.*, in the ankles and lower parts of the thigh in obstruction of the crural vein. Œdema is wanting or disappears, if the thrombus merely lines the vessel, if there exists a sufficient collateral circulation, as well as in secondary canalisation of thrombi forming complete obstructions. Hæmorrhages occur in venous obstructions only, when almost all the lateral channels are obstructed, and when thrombosis follows very quickly. Gangrene appears only when from other causes, *e.g.*, in puerperal fever, erysipelas is added. It is not a direct consequence of venous obstruction. Elevated temperature, "*œdema calidum*," is observed only in robust individuals, as in most puerperal women, not in the marasmic. Dilatation of collateral veins almost never happens: in thrombosis of the crural the collateral circulation is probably provided for by the sacral and lumbar veins. Very rarely is the obstructed vein, even the crural, distinctly known by the touch. Only obstructed cutaneous veins, *e.g.* the saphena, can usually be distinctly felt. If thrombosis exists for a long time, there results a thickening of the skin and connective tissue, even of the periosteum and bones (elephantiasis of external parts).

Consult BRAUNE, *Die Oberschenkelvene des Menschen*, 1871.

The symptoms of thrombosis of the veins of internal organs, even when very extended, and the veins belong to organs essential to life (*e.g.*, cranial sinuses, venal veins, vena portæ) are rarely so clearly defined, that it becomes possible to frame a safe diagnosis. Besides the already known consequences of passive hyperæmia (œdema, dropsy of cavities, etc.), there are causes especially to be taken into consideration (caries, marasmus, etc., in thrombosis of the cranial sinuses; puerperal inflammation of the uterus, in thrombosis of the uterine veins; cancer of the liver, severe local affections of the intestines, inflamed hæmorrhoidal tumors, inflammation of the umbilical veins of the new-born, etc., in thrombosis of the vena portæ; older inflammations with the formation of cicatrices in thrombosis of the renal veins, vena portæ, etc.). Further, dilatation of collateral channels, *e.g.*, in thrombosis of the cranial sinuses, that of emergent veins, of the

frontal, ophthalmic vein, etc., in that of the vena portæ, that of subcutaneous abdominal veins, is important. Finally, the appearance of the phenomena of embolism draws attention to its source, thrombosis.

Consult, on thrombosis of the sinuses, the more recent works of HEUBNER (*Arch. d. Heilk.*, 1868, IX., p. 417), and WREDEN (*Petersb. Med. Ztschr.*, 1869, 8. et 9. H.).

All the symptoms and consequences of thrombosis DISAPPEAR after weeks or months, if the thrombus is reabsorbed or is sufficiently canalized, or if there is an abundant formation of collateral channels.

The most important consequence of THROMBOSIS OF THE ARTERIES IS ANÆMIA of the part (*vide* p. 165). But this usually escapes observation in coagula of local origin, because then coagula are usually of gradual formation. Gangrene of the part appears later, when the thrombosis is of quick origin, without its appearance being accompanied by the establishment of a sufficient collateral circulation.

Arterial thrombosis also in many cases is innoxious through the introduction of a collateral circulation. TIEDEMANN, in the course of a year, ligated one large artery after another, without causing death. O. WEBER had a dog, in which he had, within two months, ligated both carotids and both femorals, and which was entirely well.

The special symptoms of arterial thrombosis remarkably resemble those of high grades of chronic arteritis and of growing aneurisms, and are distinguished from those of arterial embolism by the slowness of their appearance.

THROMBOSIS of the different CAVITIES OF THE HEART, especially of those of the right side, is sometimes altogether wanting in symptoms, as in most so-called globular vegetations, but sometimes furnishes auscultatory signs (thrombosis of the auricles, etc.). The antecedent condition of the heart especially (dilatation from fatty metamorphosis or old myocarditis, endocarditis), peculiar murmurs, as well as the appearance of embolic symptoms, are to be considered in the diagnosis.

THROMBOSIS OF THE LYMPHATICS is attended by no marked symptoms (*vide* DROPSY).

Thrombosis of the veins as well as of the lymphatics can exert a BENEFICIAL INFLUENCE on the organism, when, *e.g.*, they affect vessels whose roots lie in a collection of pus or ichor, since then the thrombosis by preventing resorption, imprisons, as it were, the injurious substances, and so the spread of infection to distant parts, especially the blood, is prevented.

B. EMBOLISM.

Thrombi, non-organized, gradually become softer and more rotten. In thrombi lining the walls of the vessels and partially obstructing them, the blood-stream may tear off and carry away pieces of them, or remove and transport them *in toto*. The same can happen to thrombi which wholly obstruct a vessel and are progressive in growth, if they project beyond the mouth of the vessel in which they were formed: the blood-stream which comes in contact with them, with the points of the coagula, tears them, or pieces of them away, and carries them farther on. In both cases, the pieces torn away are driven into the next narrower parts of the vessels. Sometimes large cylindrical pieces are removed (there are emboli of some

inches in length and as thick as the finger), sometimes the emboli are smaller, even visible only with the microscope.

That the coagula met with in other parts of the body are embolic and not original, is proven by many observations in the dead body and by experiment. One can often, by the form, color, and stratification of the impacted piece, be convinced, that it was torn from the coagulum of another locality. Numerous experiments demonstrate that the blood-stream is able to carry such coagula away with it, and even heavier bodies, as caoutchouc, pieces of muscle, quicksilver.

The PLACE OF SUCH SEPARATIONS from thrombi is most frequently the VENOUS CHANNEL, especially the crural vein, in which plugs are continuous out of its muscular branches; besides, there are the hypogastric, iliac, renal, jugular veins, the cranial sinuses, the right side of the heart, rarely other veins. In the ARTERIAL CURRENT the formation and separation of coagula take place especially in the aorta and its main branches, rarely in the pulmonary veins; in the left side of the heart on the mitral valve, less frequently on the aortic valves.

The CONSTITUTION or NATURE OF EMBOLI : they consist of—

1. BLOOD-COAGULA, most frequently by far, which as autochthonous or continued thrombi have so far changed their consistency that it is possible for the blood-current to tear pieces from them, and carry them away into the vessels. They sometimes as a whole play the part of emboli : e.g., as vein-stones. (The general consideration of the process of embolism is based upon the former origin.)

2. Substances, which originally stood in organic relation with the walls of bloodvessels. When this connection ceases to exist, the substances are carried farther on by the blood-stream, and act like ordinary emboli. Examples of these are found in fragments from the chalky, bony or atheromatous VALVES OF THE HEART, and from the degenerated hypertrophic inner coat of the arteries.

3. Substances, which from the beginning are formed on the inner surface of the heart and vessels : e.g., INFLAMMATORY PRODUCTS of the CARDIAC VALVES ("endocarditis ulcerosa"), carcinoma of the endocardium, veins, great lymphatics.

4. Substances, which have their origin outside of the circulatory system, but by their growth perforate the walls of the vessels, finally reach the vessels' interior and there become free : CARCINOMA and ABSCESSES, more rarely enchondroma and sarcoma of THE HEART AND VEINS.

Here BÖTTCHER'S case partly belongs : in metastatic renal abscesses elastic fibres were found which had been transported from pulmonary abscesses. (Vide Secondary New-formations.)

5. PARASITIC PLANTS AND ANIMALS, which, by their increase (bacteria, echinococcus, etc.) or wanderings, find their way into the vessels (embryos of tape-worms, distomum hœmatobium, trichina spiralis).

6. Corpuscular substances, which find their way into the vascular system : LIQUID FAT, AIR IN THE BLOOD, and PIGMENT-MOLECULES in melanæmia. Fat is absorbed in fracture of normal bones, lacerated adipose tissue, etc., and is not infrequently found in the veins, whence it passes into the general mass of blood, and especially into the lungs. Air enters the circulation through wounds of the veins, sometimes also in a manner unknown. Pigment-molecules in melanæmia are probably always taken up by the veins from the spleen.

7. A number of substances, which do not enter the circulation except in SOLUTION, and are deposited in definite localities : METASTASES. Here belong :

a. Normal substances of the organism, which on account of lessened excretion through the veins and lymphatics, accumulate in the general circulation and are deposited in various parts of the body : especially the coloring matter of the bile.

b. Normal substances of the body, which in various diseases are not normally transformed or excreted, or which are formed in increased quantity : thus, uric acid and its salts which are deposited within and around the joints in gout.

c. Substances, which accumulate in the blood in too great quantity and are not normally transformed or excreted : thus lime-salts which, in osteomalacia, extensive caries of the bones, inflammation of the bones, are deposited in the kidneys, lungs, stomach, etc. (" chalky metastases ").

d. Many medicaments, as silver-salts, which are deposited in the skin and renal tissues, and salts of lead, in the gums.

CAUSES OF EMBOLISM.

The PREDISPOSING causes are given above.

The EXCITING CAUSES are, during the existence of ordinary thrombi, in particular, sudden movements, quick rising out of bed, sudden changes of position, straining at stool, coughing, friction or pressure on thrombosed vessels. For the remaining emboli, not consisting of blood, for the most part no exciting causes are necessary.

THE LOCALITIES INTO WHICH EMBOLI ARE FORCED are : with respect to the emboli formed in venous blood, as in the veins of the great circulation and in the right side of the heart : in the pulmonary arteries and their branches (emboli very rarely remain fixed in the heart itself) ;—with respect to the plugs having their origin in the arterial blood, as in the pulmonary veins, in the left side of the heart, in the arteries : the arteries of the body ;—with respect to the coagula formed in roots of vena portæ : the hepatic branches of the portal vein.

The DIRECTION OF EMBOLI of large size is a tolerably constant one. They usually tend toward the posterior and lower parts of an organ, in obedience to the law of gravitation. They take the direction of the main current, and pass into the lateral branches only when the force of the current in the main vessel is very small, or the vessel is already obstructed by emboli, etc. From only exceptional and unknown causes do they enter branches perpendicular to the main vessel, *e.g.* into the cœliac axis, the coronary arteries of the heart, the bronchial arteries.

Emboli from the left side of the heart usually pass into the thoracic aorta, and from here most often into the abdominal aorta and renal arteries, as well as into the iliacs and their branches; somewhat less often into the carotids, rarely into the subclavians. Of the carotid, renal, and iliac arteries, those of the LEFT SIDE almost exclusively are affected by embolism, since in them the chief current has a more direct course.

Emboli from the veins pass most often into the lower lobes of the lungs, except when the latter are infiltrated or compressed, or when their larger branches are already obstructed by emboli. The cause of the frequent occurrence of emboli in the lower lobes is this, that the embolus moves more slowly than the blood-stream and adheres to the walls, thus to the lowest part of the wall of the trunk of the pulmonary artery. Emboli occur most frequently in one and the same branch of the pulmonary artery. They affect much oftener the right pulmonary artery, because its current is

greater, because the left is covered by the aorta, and its stream is thereby somewhat hindered; finally, because most sick people lie on the left side, which therefore somewhat contracts the left half of the thorax.

If a vessel be obstructed by one or more emboli of not too great size, subsequent embolism will mostly affect the same vessel, because its walls are separated by the first emboli and become more than normally distended.

In rare cases emboli travel in a DIRECTION OPPOSITE to that of the blood-stream, *e.g.* from the right ventricle or superior cava into the hepatic veins. This is the case in those diseases of the respiratory apparatus where the normal negative pressure in the thorax is temporarily or permanently changed into a positive pressure, as in all diseases characterized by cough, in capillary bronchitis, in pleuritic effusions, etc.

After MAGENDIE, CRUVEILHIER, FRERICHS, and COHN had experimentally demonstrated that bodies (quicksilver) introduced into the jugular vein could reach the hepatic veins by means of RETROGRADE CURRENTS, HELLER (*D. Arch. f. klin. Med.*, 1870, VII., p. 127) showed the same, by an experiment with wheat-grits and by a pathologieo-anatomical observation in man (cancer of the cæcum and various lymph-glands; cancerous embolus in a hepatic vein). I myself saw, attention having been drawn to it by THIERSCH, in two cases of thrombosis of the jugular vein after surgical operations, hepatic without pulmonary abscesses, which were explained in similar manner.

Emboli, from the beginning, OBSTRUCT THE VESSEL WHOLLY OR ONLY IN PART. The embolus is usually arrested at a part where the vessels divide, or where the diameter of the vessel is suddenly reduced by giving off branches. The larger plugs usually go to the point of division, so that they are, at the same time, somewhat forced into both branches. At first they lie loose in the vessel (which distinguishes them from autochthonous thrombi), and do not at first commonly obstruct the vessel completely in any branch. A little blood still passes by them, although far less than before, so that a stagnation always results behind the embolus. New precipitates begin before and behind the embolus, so that it becomes encapsuled by fresh coagula, and yet a slight current still remains. If the embolus is very large and cylindrical and soft, it obstructs at first the arterial branches completely, the artery contracts about it, and behind it is entirely emptied of blood; before the embolus, *i.e.*, toward the heart, a secondary thrombus is formed, as in the case of ligature, as far upward as the next larger lateral branch.

In obstruction of very small vessels in the frog, coagulation is uniformly absent; sometimes also in man, because the influence of the vessel's walls to prevent coagulation surpasses that of the walls to promote it.

The larger emboli naturally remain in the larger, the smaller only in the smaller vessels; the smallest, finally, are usually arrested in the first capillary net-work, which they have to pass, more rarely to be held in another: CAPILLARY EMBOLISM. These embolisms concern sometimes the capillaries only, sometimes at the same time also the smallest arteries belonging to them. That both the smallest vessels and the capillaries may become embolized has not only been proven by numerous autopsies, but experiments with quicksilver, carbon, starch, fat, wax, etc., have also demonstrated the possibility of this occurrence.

Emboli having their origin in the veins, usually remain fixed in the variously thick branches of the pulmonary arteries. The smallest emboli of the veins, however, are only arrested in the pulmonary capillaries, or pass the lungs, and remain fast in the next following capillary region (liver, spleen, kidneys, etc.). How they pass the lungs is explained by the fact that in many places in the lungs, a direct communication exists between the arteries and veins, which is seen when, anywhere, in consequence of a congestion, the intervening branches are distended (*vide* p. 148).

CAPILLARY EMBOLI most frequently have a PRIMARY origin, by separation of the finest particles of a thrombus. Their origin is less often SECONDARY from a non-capillary, especially a lining embolus, from which very fine particles become separated. Emboli arising from coagulated blood are characterized by their external appearance, and great resistance to all reagents.

CHANGES IN THE EMBOLUS AND IN THE WALL OF THE VESSEL make their appearance if the functional disturbances caused by the embolism are not so great as to cause instant death. In rare cases emboli are ABSORBED, and the vessel again becomes free. CANALISATION of the embolus is almost as rare, leading to the permeability of the obstructed part, and sometimes giving rise to secondary emboli. Or they become ORGANIZED like thrombi (*vide* p. 191), and so become altogether or in part harmless. Emboli may too become SOFTENED, and thereby lead to the formation of secondary emboli. Finally, they rarely become HORNY or CALCAREOUS. By means of most of these processes the channel of the vessel can, at least in part, be re-established.

CHANGES AFFECTING THE WALL OF VESSELS are, in the first place, dependent upon the absence of the CIRCULATION. More recent experimental investigations show that bloodvessels, by a long interruption or arrest of the circulation in them, become as incapable of function as muscles and nervous apparatus, when deprived of blood. At first the vessels are dilated; after a longer time there appears œdema with emigration of colorless blood-corpuscles; after a still longer time hæmorrhages, the circulation stops altogether and the vessels die. At first the veins, then the capillaries, finally the arteries, become the seat of these disturbances.

COHNHEIM has experimentally investigated the above-described consequences of the exclusion of the blood from a vascular region, with respect to the wall of the vessel itself. After ligating the whole tongue in a frog, the circulation immediately ceased. The vessel-wall, even after four or five days of total ligation, showed no morphological changes. When, from a few to twenty-four hours after, the ligature is removed, the circulation is very quickly re-established : the vessels are immediately thereafter largely dilated, the blood-stream very quick; but soon the arteries first contract, then the veins, and after one to two hours the normal condition is restored. If, on the other hand, the ligature be loosened, not until after about forty-eight hours, the dilatation of the vessels and velocity of the stream will be still greater ; then the arteries contract, the blood flows more slowly ; but the veins remain dilated, and from them and from the capillaries the white blood-corpuscles, from the latter also red corpuscles, wander out in large numbers. If the ligature be loosened after sixty hours, numerous capillary hæmorrhages will be found, less from the smallest veins. After four or five days of ligation the tongue becomes necrotic. Similar results followed total ligation of the ear, testicle, and kidney in the rabbit. (Similar changes arise from arrest of the venous flow.)

In the second place, the changes in the vessel-wall depend upon the MECHANICAL OR CHEMICAL CHARACTER OF THE EMBOLUS. Indifferent emboli effect no, or only trifling, changes in the vessel-wall (thickening, sometimes growth with the surrounding tissues). If, however, the embolus is from a foul or gangrenous part, it may give rise to a septic or gangrenous inflammation of the vessels, which extends to a varying distance into the sur-

rounding tissues. If the embolus has rough surfaces, *e.g.* in separated calcareous pieces of the valves of the heart, the inflammation is more violent ; suppuration is a not infrequent result.

THE CHANGES IN THE ORGANS whose arteries are obstructed by embolism depend upon the embolus itself (its size, number, its power to create mechanical or chemical irritation, etc.), the kind of vessels (functional or nutritive vessels), the arrangement of the arteries, the re-establishment of a collateral circulation, and the structure of the organ itself.

More recent EXPERIMENTAL INVESTIGATIONS concerning these relations yield the following results : The experiments were made on the frog, especially its tongue, which was at the same time examined microscopically, and were conducted by the injection of an emulsion of wax, colored black by lampblack, into the heart or aorta.

At first, the arteries are closed and a collateral circulation is established in the surrounding tissue (*vide* p. 174). At the place of the obstruction the artery is usually bulged out, distinctly narrower before and behind. The contents of the vessel no longer move, in front of and behind the globules of wax : in the former locality as far as the lateral branches, in the latter for a varying distance. If the embolus comes quickly, with the swiftness of the blood, to its locality, there is before and behind it a column of red blood with few colorless blood-corpuscles ; but if slowly, it is driven forward by successive thrusts, and thus a gradually increasing obstruction is formed in the blood-stream, the vessel both before and behind the obstruction is filled with plasma and colorless corpuscles. (A coagulation of the blood does not occur in the frog.)

The capillaries and veins supplied by the obstructed arteries, act differently. Between the plug and the capillaries there is given off an arterial branch, which communicates with a branch of another artery (collateral or anastomotic), thus through these a sufficient quantity of blood is supplied to the peripheral region once served by the obstructed artery, and its circulation goes regularly on. The function of the closed artery also is destroyed above and below as far as the lateral branch. In like manner are the capillaries affected by embolism. If, on the other hand, such an arterial anastomosis is wanting behind the obstructed terminal artery, the blood behind the obstruction stands absolutely still, as well in the arterial branch affected as in the capillaries supplied by it ; also in the efferent vein until it meets with another vein which is supplied by a non-obstructed artery. After a short time there appears in the streamless vein a recurrent movement into the capillaries, and beyond these into the artery, at first uniform, later rhythmical. This gives to the part after a little time the appearance, to the unaided eye, of a dark-red, sharply-defined wedge. Still later, a hæmorrhage here occurs, and a HÆMORRHAGE INFARCTUS arises, visible to the naked eye.* (The bleeding is explained by the changes which the vessels, especially the capillaries of the embolized region, have experienced through the interruption of the regular blood-supply.)

The above-mentioned experimental results correspond in all essential particulars with pathologico-anatomical facts.

Four different effects are therefore ascribed to emboli.

Emboli are altogether WITHOUT EFFECTS : they remain fixed, organize and grow with the wall of the vessel ; the parenchyma behind the obstruction remains normal. This is the case, when behind the embolus a sufficient

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* Consult PREVOST et COTARD, *Ramollissement cérébral.--Gaz. Méd.*, Paris, 1866. —[ED.]

arterial anastomosis already exists, or is established in a very short time. Examples are found, especially, in the larger branches of the pulmonary artery, the arteries of the brain anteriorly and in the circle of Willis, less often the mesenteric arteries, etc.

Or, behind the embolus, GANGRENE appears in its different forms : this is oftenest the case in the extremities in their whole thickness, or only in the skin, and in the brain.

If the main branch supplying an organ, or many large branches of it, become WHOLLY OBSTRUCTED, and nutritive blood is no longer supplied, nor a sufficient collateral circulation is quickly established, GANGRENE of that organ follows. Gangrene is the effect of anæmia. Besides, through stasis in the capillaries and veins, a high degree of congestion and even extravasation of blood may take place. The extent of the gangrene is always smaller than would be expected from the size of the obstructed artery. The gangrene is for the most part moist and odorless. In the brain and spinal cord it exists as the so-called softening, mostly white. In the surrounding tissues there not infrequently exists a high degree of collateral hyperæmia and even numerous hæmorrhages, the latter especially in the brain. Gangrene very rarely occurs in the parenchyma. COHNHEIM (l. c. p. 76) saw total embolism of the renal artery, and consecutive total necrosis of the kidney.

Or HÆMORRHAGES arise : superficial bleedings, or bloody infiltrations in extended organs, hæmorrhagic infarctions in parenchymata. Such occur most often in the lungs,. spleen, kidneys, less frequently in the brain, retina, intestinal tract, never in other organs. Both processes, gangrene and hæmorrhage, occur only in organs where, between the obstruction and the capillaries, insufficient, inconstant, or no arterial anastomoses exist. Besides, hæmorrhages can occur only in organs where the veins are without valves. These conditions are found especially often in the lungs, spleen and kidneys.

True terminal arteries are present in the organs named, in the retina, and interior of the brain. Cerebral anastomoses, at a distance from the circle of Willis, are inconstant and very small. They are constant but much too small in the last arterial branches of the pulmonary arteries, the inter-alveolar arteries. According to RIND-FLEISCH (*Lehrb.*, 1873, p. 395), not only all the main branches of the pulmonary artery, but also those entering the lobules, running between two neighboring lobules as well as finally the smallest branches are terminal arteries.

Hæmorrhagic infarctions are more often peripheral than central; they are black-red, firm, homogeneous, or, according to the structure of the organ, horny, striated, etc. In their farther progress they grow pale from the centre outward (or this was pale from the beginning), and may become absorbed through fatty metamorphosis with subsequent scar. They less frequently entirely, or at points pass into suppuration, or ichorous transformation, or gangrene.

Hæmorrhagic infarctions were until recently regarded as hæmorrhages in consequence of high grades of collateral hyperæmia : it was believed, that through the sudden obstruction of numerous capillaries and of the smallest arteries supplying them, there arose a stronger hyperæmia and rupture of the central and peripheral capillaries, veins and smallest arteries (especially in yielding tissues, like the lungs, spleen, brain), and coagulation of the extravasation. COHNHEIM has shown, that they arise from a recurrent movement of the blood in the formerly streamless veins, and from hæmorrhages in the district occupied by their capillaries. With respect to this, direct observation above all bears testimony ; farther, that the infarctions do not appear immediately after the embolism, but only a little time after ; then that in hæmorrhagic infarction of the lungs the arterial embolus is not situated exactly at the point of the infarction, but somewhat to one side. Besides, there is a fre-

quency of infarctions in the organs named above: emboli, when their origin is in
the heart and are not too large, are transported everywhere, but in all parts, except in
the organs above-mentioned, anastomoses are present in the arterial system and
there are no terminal arteries. The ABSENCE OF HÆMORRHAGIC INFARCTIONS in
the liver has its explanation in this, that there is almost no source of simple
mechanical emboli in the portal vein. The non-appearance of a hæmorrhage in
other cases is in different localities explained in different ways. Behind the embol-
ism of a large terminal artery the blood in the corresponding large veins may coagu-
late: thus in the larger branches of the pulmonary and renal veins. The situation
and position of the affected organ may also be of influence: in the brain, *e.g*, the
recurrent venous stream is much more easily established, when it is favored by
gravity. Farther, the energy of the heart's contractions is of influence: *e.g*., in
inflammation of the aortic valves with cardiac hypertrophy of the left side, when
positive pressure also is more considerable in the veins, a quicker infarction is possi-
ble. In partial embolism, as well as with the existence of too small anastomoses,
there is still in the embolized part a circulation very weak in quantity, velocity
and pressure, which circulation may indeed render difficult the recurrent venous
stream, but not sustain nutrition (COHNHEIM).

Or, finally, there arise METASTATIC ABSCESSES. These occur through
embolism acting mechanically, but especially by chemical means, namely,
bodies impregnated with putrid material. They mostly exhibit in trans-
verse section three layers: a purulent, or necrotic centre, into which the
occluded artery leads and the veins filled with coagula from the periphery;
an infarcted mass of tissue saturated with blood-corpuscles and fibrin; an
external zone of collateral hyperæmia. Embolic abscesses are of various
sizes and forms. The larger occur only in the lungs and liver; in other
organs they are about the size of a millet seed. They are mostly globular,
less frequently longitudinally striated, etc. They occur in the interior as
well as (like infarctions) on the surface of organs.

According to COHNHEIM, embolic abscesses are dependent either upon obstruction
of the capillaries or smallest arteries; or, as in the lungs and liver, upon plugs in
arteries which behind these are still supplied with numerous anastomoses. In both
cases there is no true interruption of the circulation, but a purulent inflammation,
which is consequent upon the presence of an injurious foreign body. The size of
the abscess, its course, etc., are dependent only on the size and the injuriousness of
the embolus, and on the liability of the organ to damage.

If the vessel be NOT COMPLETELY OBSTRUCTED by the embolus, as is the
case especially in emboli of firmer consistence, which cannot adapt them-
selves to the inner form of the vessel, also as is usual in the case of
emboli fixed at the point of division of the artery, then the affected arte-
rial region becomes only transiently anæmic, and only until a sufficient col-
lateral circulation is established. The open interval either remains, or
becomes closed by supplementary deposits of fibrin.

CAPILLARY EMBOLISMS frequently are of no importance, when their num-
ber in the same capillary district is not too great, since only the capillary
affected is closed; less often are they the cause of punctiform extravasa-
tions. The latter are explained by the changes of the vessel-wall, which
arise during the obstruction, but they do not appear till after the removal
of the embolus.

The STRUCTURE OF THE ORGAN exercises an influence in various ways by
means of its changes from embolism of its nutrient vessels. Under all
circumstances there arise acute or chronic disorders of nutrition. The
firmer the tissue, the less the liability to hæmorrhages and to the develop-
ment of an abundant collateral circulation; the softer it is, the more easily
do hæmorrhages occur, and sufficient collateral currents. The more vascular

it is, so much the earlier does gangrene appear in absence of a collateral circulation. The most extensive and quickest destruction of tissue follows embolism of the capillaries in soft textures (lungs, liver, spleen, brain); there arise METASTATIC ABSCESSES. The tissues are destroyed more slowly in the kidneys and still more so in the skin: here there are formed firm, yellowish white, purulent plugs, so-called FURUNCLE. In the bones, necrosis takes place only after a long time, the dead parts gradually becoming loosened, so called SEQUESTRA.

In ORGANS with a DOUBLE SYSTEM OF VESSELS, functional and nutritive, embolism of the nutritive vessels affects the texture and function at the same time, because function is possible only during normal nutrition. In embolism of the vessels of function, normal nutrition remains; but the inactive parenchyma often becomes atrophied, not infrequently with hypertrophy of the interstitial connective tissue. Nutritive blood can act vicariously for the functional, but not *vice-versa*.

The COLLATERAL CIRCULATION of parts obstructed by embolism is, as said above, of the greatest importance with respect to the future of the organ affected. The quicker it is established and the more efficacious it is, the less the anatomical and functional disturbance. It arises either from other branches of the embolized vessel, or from other vessels, but of the same kind, or finally from vessels of an altogether different character: both the former modes are seldom found in the brain where only large and very small, but no intermediate anastomoses occur; the latter mode occurs in the lungs, in obstruction of the pulmonary artery on the part of the bronchial arteries. In diseased vessels a collateral circulation is usually less complete. The collateral circulation already established can thereby in turn be interrupted, so that the primary coagulum gradually grows toward the heart.

In a case cited by VIRCHOW, the main vessel of the whole pulmonary lobe of a dog was totally obstructed by embolism, by injection of large particles into the jugular vein. When the animal died, after a half year, the autopsy showed that while an injection-mass could not be driven from the right side of the heart into the affected lobe, the most delicate injection of the pulmonary vessels could be obtained from the very dilated bronchial arteries. The lung itself was normal.

The INFLUENCE OF EMBOLISM ON THE WHOLE ORGANISM depends: upon the interruption or abolition of certain functions essential to the organism (embolism of the pulmonary artery, of the portal vein, of the cerebral arteries); upon irritation of the sensory nerves in the affected organ and their reflex action on other parts and functions (chills, fever, convulsions, neuralgia); upon the sudden diminution of the current, and the recurring congestion and plethora (congestion, syncope, asphyxia); upon softening, gangrene of the organ; upon the sequelæ of absorption (septicæmia), etc.

SYMPTOMS OF EMBOLISM.

Autochthonous thromboses differ from embolisms in that the consequent phenomena arise slowly, while in large embolic obstructions WITH SHOCK, the consequences of the cut-off blood-supply appear in a day. If, *e.g.*, embolism affect one of the larger arteries of the brain (*art. fossæ Sylvii*), apoplexy immediately follows, *i.e.*, paralysis of the part of the brain affected; if it affect a large branch of the pulmonary artery, there appears suddenly the danger of suffocation; if one of the coronary arteries of the heart, there follows acute paralysis of the heart's movements, pain, feeling of impending annihilation with retained consciousness. A great portion of

the sudden amauroses in pyæmia, puerperal fever, acute rheumatism of the joints, are of an embolic nature: their immediate cause is the acute endocarditis often complicating those processes. In embolic obstruction in an extremity, there suddenly appear severe pain, a feeling of numbness, sometimes a chill, sometimes loss of the sense of touch, with general pains, paleness, and a feeling of cold, weight and paralysis of the muscles. The pulse beneath the obstructed part is no longer felt, above it beats with so much stronger impulse.

With respect to the locality of attack, the already mentioned frequency of embolisms on the left side is important. Embolic paralyses of the brain are examples, because the left hemisphere is commonly affected, mostly the right half of the body; embolic paralysis of a lower extremity is usually on the left side.

If death does not immediately follow embolism, a recovery can take place after the first severe symptoms, which are often attended by a chill. Even the most severe and most striking symptoms (paraplegia, hemiplegia, motor, sensory paralyses of an extremity, attacks of dyspnœa, symptoms of angina pectoris, etc.), can, after minutes and hours, entirely disappear, if the terminal arteries be not obstructed, and if with corresponding quickness a COLLATERAL CIRCULATION be established. This can rarely be entirely overlooked during life. The disorders, which are manifested as external symptoms in the obstructed region, are therefore very different. Ischæmia is often so considerable, that the veins also immediately lose their power to carry the blood onward. In the extremities, especially, a bluish-redness appears soon after the first paleness, also some œdema, small hæmorrhages, even the formation of vesicles; sometimes true venous thrombosis. On the other hand, through obstruction of a small branch, so much blood may flow into the vessels near by, as to give rise to symptoms of inflammation.

There may, e.g., be an embolic obstruction in one carotid within the carotid canal, and a resulting paralysis of one side; but it will just as quickly disappear, since the blood soon becomes supplied from the other side through the circle of Willis, and also from the vertebral and basilar arteries. But if the embolus affects the region above the circle of Willis, e.g., in the art. fossæ Sylvii, hemiplegia follows.

The usual termination, however, in the case of large and complete arterial obstructions, especially of the brain and extremities, is SOFTENING or GANGRENE, which for weeks and months proceeds continuously to the point of obturation.

In parts poorly supplied with nerves (liver, spleen, kidneys, most mucous membranes) the more important symptoms are wanting, or the embolisms are entirely without symptoms. Bloody expectoration frequently appears in consequence of collateral hyperæmia in the lungs dependent on embolus, in the kidneys, occasional hæmaturia. Symptoms of partial pleurisy, and peritonitis, are frequently present as a consequence of peripheral infarctions in the lungs, liver, and spleen.

In embolism of the mesenteric arteries, there occur copious, even exhaustive intestinal hæmorrhages, abdominal pain (sometimes like colics and very intense), finally tympanitic distention of the abdomen and peritoneal exudation (COHN, OPPOLZER, GERHARDT, KUSSMAUL, HEGAR).

BOHN (Jahrb. f. Kderheilk., 1868, I., p. 391) holds WILLAN's erythema nodosum and SCHÖNLEIN's peliosis rheumatica, also HUETER's (Klin. d. Gelenkkrkh., 1870, p. 98 ff.) polyarthritis synovialis acuta (acute rheumatism of the joints), to be of embolic nature.

According to BASTIAN (*Brit. Med. J.*, Jan., 1869), obstruction of small arteries and capillaries by white blood-corpuscles in the gray matter of the brain in intense febrile disease, is the cause of the delirium, and stupor, and other symptoms of the typhoid state.

Farther important differences in the symptomatology arise, according as the embolism affects the vessels of NUTRITION or FUNCTION. With respect to the latter, the pulmonary artery chiefly is of interest.

Embolic obstructions of its smaller branches, are of all embolisms the most frequent, but almost always entirely without symptoms. Also when larger branches of the pulmonary artery become obstructed by emboli, no symptoms appear. In the dead body the affected parts of the lungs are sometimes not essentially changed, because the bronchial vessels dilate vicariously, sometimes are anæmic, collapsed, and somewhat emphysematous; sometimes hæmorrhagic infarctions are found, surrounded by collateral hyperæmic tissue. Only when numerous small branches of the pulmonary artery are closed at the same time or soon after one another, or when a very large branch is obstructed, when a large part of the lung is thus suddenly deprived of blood and on that account so much the more blood flows into other parts, do marked symptoms appear. Suddenly apnœa appears, and after longer duration, in consequence of collateral hyperæmia, acute œdema. Percussion is normal, but when œdema exists, auscultation reveals fine rales. The inspiration is free. The pulse is sometimes small, the skin and mucous membranes are very pale; the second sound, and the heart's impulse are increased; the extremities become cold, the muscles weak. Death follows from anæmia of the spinal cord. In the autopsy both halves of the heart are found in diastole, the left cavities and the pulmonary veins empty, the right cavities filled with blood, the cardiac veins strongly distended.

SUDDEN DEATH IN SEVERE EMBOLISM OF THE PULMONARY ARTERY depends upon the want of blood-supply to the brain and medulla oblongata. The phenomena of death from the indirect interruption of the arterial blood supply to the great nerve centres, are altogether identical, and the mechanism of death is in both cases the same. In this it is a question neither of suffocation, nor of paralysis of the heart. In extensive embolisms of the pulmonary artery, the first quite constant phenomenon is the extreme paleness of all visible parts of the body (conjunctiva, gums, lips). The white brain matter is entirely empty of blood; the veins and venous sinuses of the brain are filled with blood. This paleness is immediately followed by constant tetanic extension of the limbs, involuntary evacuation of the urine and feces, and very deep inspiratory movements (PANUM'S experiments).

The SYMPTOMS OF CAPILLARY EMBOLISM have until now been almost only accessible to ophthalmoscopic examinations.

Embolism of the pulmonary capillaries with great quantities of air or of liquid fat also lies at the foundation of a number of CASES OF SUDDEN DEATH. The causes of embolisms of air are injuries (usually wounds, rarely ulcerations, etc.) of the larger veins in the lower part of the neck, of the upper part of the thorax, of the axilla, rarely of the upper, almost never of the lower extremities, with aspiration of external air: of embolisms of fat, extensive lacerations or contusions of the subcutaneous adipose tissue, and especially of the marrow of bones. From embolism there arises an insufficient decarbonization of the blood, and especially a stoppage of the supply of arterial blood to the spinal cord. Small quantities of air and of fat are probably diffused, oxidized, etc., and for the most part therefore uninjurious.

Consult Amussat, *Rech. s. l'introduct. accid. de l'air dans les veines*, 1838 ; Poiseuille, Mercier, Beck, O. Weber. *Handb.*, p. 95 ; the Author, *Arch. d. Heilk.*, III., p. 241 ; VI., pp. 146, 368, u. 481 ; Busch, *Virch. Arch.*, XXXV., p. 321.

Besides, concerning the symptoms of embolism of putrid and gangrenous material, concerning "metastases," *vide* Gangrene, Pyæmia, etc.

The symptoms of embolism of the lymphatics are not yet known. Besides, embolism can occur only in subordinate proportions, because those vessels enter the lymph-glands before terminating in the larger branches, especially the thoracic duct.

Consult, on the other hand, the opposing experiments of Schweigger-Seidel, *Stud. d. phys. Inst. zu Breslau*, 1861, 1. H., p. 67.

The diagnosis of embolism depends : 1, upon a knowledge of the sources of embolism ; 2, upon the proof of the diminution, or of the sudden entire disappearance of the thrombosis serving as a source ; 3, upon the appearance of atypical chills, with or without enlargement of the spleen, with complete remission of the fever ; 4, upon the sudden appearance of a series of disturbances in the function of an organ, which find in embolism their full, if not also their exclusive explanation, and which usually appear from the first with all their intensity, and either lead quickly to an unfavorable termination, or quickly or slowly, in their farther progress, assume a somewhat more favorable course.

4. HÆMORRHAGE.

(Hæmatorrhœa s. Profluvium Sanguinis.)

C. J. Meyer, *System. Handb. zur Erkenntniss und Heilung der Blutflüsse*, 2 Bde., 1804 et 1805.—Virchow, *Virch. Arch.*, 1847, I., p. 379 ; Würzb. Verh., VII. ; *Handb. d. spec. Path. u. Ther.*, I., p. 227 ; *Die krankh. Geschwülste*, I., p. 128.—Pestalozzi, *Ueb. Aneur. spuria der kleinen Gehirnarterien und deren Zusammenhang mit Apoplexie*, Würzburg, 1849.—Paget, *Lond. Med. Gaz*, 1850.—Stich, *Ann. d. Berl. Char.*, 1852, III., p. 192.—Moosherr, *Ueb. d. path. Verh. d. kl. Hirngeff*, 1855.—Beckmann, *Virch. Arch.*, 1861, XX , p. 227.—Rindfleisch. *Arch. d. Heilk.*, 1863, IV., p. 347 ; *Experimental stud. üb. d. Histol. d. Blutes*, 1863.—O. Weber, *Handb. d. allg. u. spec. Chir.*, 1865, I., p. 119.—Consult besides the surgical works of Bell, Boyer, Velpeau, Billroth, Erichsen, Gross, Holmes.

By the term HÆMORRHAGE is understood the escape of blood, through various pathological conditions, from its natural reservoirs (EXTRAVASATION). This takes place as well in the heart as in the arteries, veins, and capillaries ; hence we have CARDIAC, ARTERIAL, VENOUS, and CAPILLARY hæmorrhages. PARENCHYMATOUS hæmorrhages are those which simultaneously proceed from numerous small arterial and venous branches, and capillaries.

Every LARGE extravasation of blood, *i.e.* of serum and blood-corpuscles, also every escape of a large quantity of red corpuscles outside of the vessels, presupposes a RUPTURE OF THE VESSELS : "HÆMORRHAGE PER RHEXIN." Since this is often not demonstrable, especially almost never with respect to the capillaries, rarely with respect to the small arteries and veins, the demonstration in doubtful cases of a great quantity of RED blood-corpuscles outside of the vessels is sufficient. The SMALLER and smallest hæmorrhages, especially from the capillaries and smallest veins, may occur WITHOUT VISI-

BLE INJURY TO THE VESSELS. The blood-corpuscles leave the vessels, accord-
ing to some, by a kind of trickling process: " HÆMORRHAGE PER DIAPEDI-
SIN "; according to others, through very fine, preformed openings in the
walls of the vessels (stomata): BLEEDING PER ANASTOMOSIN.

DEMETRIUS assumed, besides the three named kinds of hæmorrhage, one *per
diabrosin* (by ulceration, etc.), and another *per diæresin* (by wounds, etc.).

With res' ect to the form and manner of the occurrence of HÆMORRHAGES THROUGH
UNINJURED VESSELS, opinion is still divided. According to STRICKER, *Wien. Sitzgsber.*,
1865, the process is an ACTIVE one : the capillary wall, which, according to him, is
protoplasm in tubular form, and capable of independent alternate contraction and
dilatation, takes up the blood-corpuscles and forces them out. According to COHN-
HEIM (*vide* Inflammation), the process is a PASSIVE one : the increased blood-pressure
dilates the (according to him) preformed openings in the vessel's wall, and through
these the blood-corpuscles are pressed out.

Rupture of the heart and bloodvessels affects in most cases ALL THE
TUNICS or membranes. Only in the arteries, especially the aorta and in
the arteries of the brain, does it happen, that only the intima and media,
under these conditions always degenerated, are ruptured, while the adven-
titia remains uninjured, and that the blood accumulates in the spaces be-
tween the latter and middle coat (so-called DISSECTING ANUERISM).

Since the external surface of the vessels in almost all parts is con-
tinuously connected with the parts surrounding them, a great hæmorrhage—
if we except those upon the surface of the body and in the cavities—is
only possible, when the blood can collect between the tissues and the ves-
sel, as in parts which are dense, or when the surrounding parts are at the
same time lacerated, as happens in almost all the softer organs. In the
smaller and smallest hæmorrhages lacerations of this kind need not occur,
since the blood-corpuscles pass into the surrounding lymphatics (lymphatic
sheath), into the preformed spaces of the connective tissue and into the
lymphatic radicles, and, under certain circumstances, between and into
epithelial and glandular cells.

Hæmorrhages are distinguished as external and internal, with respect to
the LOCALITY OF THE EXTRAVASATION. EXTERNAL HÆMORRHAGES are those
which occur on the surface of the body or on the surfaces of mucous mem-
branes lying near it and visible (nose, mouth, vagina, rectum). With
respect to hæmorrhages on the surface, if they occur slowly with frequent
repetitions they receive the name of BLOODY FLUXES. They occur on the
surface of the skin, when normal (bloody sweat), as well as from wounds
and ulcers, but especially on mucous membranes, rarely from gland-ducts.
INTERNAL hæmorrhages are those which occur in pre-existing cavities and
canals, sometimes in the parenchyma of parts, and usually do not extend
from these, or to a slight distance, or only after some time to the surface.
From this it appears that no sharp boundary exists between external and
internal hæmorrhage.

The escaping blood is either PURE, or—and in all proportions—MIXED
with secretions and excretions (bloody urine, stool, tears, sweat), or with
exudates (so-called hæmorrhagic exudations).

The following kinds of hæmorrhage are determined by the RELATION OF
THE EXTRAVASATION TO THE TISSUES. If the hæmorrhage is small, more
superficial, and exercises little pressure upon the tissues or slightly lacer-
ates them, it is termed SUFFUSION, hæmorrhagic infiltration, and if puncti-
form, ECCHYMOSIS. If the effusion of blood is large and connected with
great separation of the tissues, with little or no destruction of them, they

are called HÆMORRHAGIC INFARCTIONS; or, if the effused blood forms a tumor on a surface, BLOOD-TUMORS, BLOOD-BOILS, HÆMATOMATA. If blood is effused in large quantity and the tissues are destroyed, it is known as a HÆMORRHAGIC FOCUS, BLOOD-SLOUGH.

HÆMORRHAGES IN VARIOUS PARTS OF THE BODY receive names by combining either "HÆMO," or "HÆMATO," or "RHAGE," with the name of the part: e.g., in the uterus as hæmatometra (accumulation of blood in the uterus), or metrorrhagia (flow of blood out of the uterus); by hæmatothorax is understood hæmorrhage into the pleural cavities, by hæmatocele that into the vaginal membrane of the testicles, by pneumorrhagia hæmorrhage into the lungs. Besides, the words hæmaturia, bloody urine, hæmatemesis, bloody vomit, hæmoptysis or hæmoptoë, bloody sputa, etc., are in common use. By PURPURA and PETECHLÆ (spots similar to those caused by flea-bites) is understood, small, purple-red, rounded effusions of blood in the skin; by MELÆNA, the escape of black blood by vomiting (or stools); by HÆMORRHOIDS, hæmorrhages of the rectum; by sedes cruentæ bloody stools, by EPISTAXIS bleeding from the nose. Large hæmorrhages in external parts, especially of the extremities, where they are connected with an otherwise normal artery, are called FALSE or TRAUMATIC ANEURISMS.

For hæmorrhagic foci, or for all kinds of hæmorrhage many use the word APOPLEXY.* This word, however, refers only to the sudden interruption of the function of an organ, and since this is very frequent in the brain, but not always dependent on effusions of blood, the word is better used in its literal sense.

The QUANTITY OF EFFUSED BLOOD varies in every conceivable degree. In many cases so great a quantity of blood is poured out in the shortest time, that death follows within a few seconds: e.g., in rupture of the heart, and of the larger, mostly arterial, rarely venous vessels (bursting of aneurisms, corrosion of the gastric arteries from ulceration, etc.) — apoplexy in its old sense. Or there happens an effusion of blood only by drops: stillicidium sanguinis, or staxis, as in the nose, intestines, etc. Or, only single blood-corpuscles appear by diapedesis, or through preformed very fine openings through the capillary wall or walls of the smallest veins, so that the hæmorrhage is recognizable only through the microscope: this happens in congestive and in mechanical hyperæmia (vide p. 180 et 186), in hyperæmia of inflammation, in primary hæmorrhagic exudations.

Hæmorrhages with escape of blood by drops are sometimes visible on the surface of granulations and villous vascular new-formations (e.g., cauliflower growths in the vagina) to the naked eye. They occur, according to VIRCHOW, sometimes also on the surface of large aneurisms, e.g., of aneurisms of the arch of the aorta, when they have pierced the sternum.

THE CAUSES OF HÆMORRHAGE.

They affect normal tissues as well as new-formations.

1. FROM FORCES ACTING EXTERNALLY TO THE VESSELS. Here are classed the different WOUNDS of VESSELS, cuts, stabs, and injuries of all kinds (most of the accidental or intended injuries of the soft parts of the trunk and extremities, contusions, bruises, etc.; similar injuries of the bones: fractures, etc., of them; cephalhæmatoma; hæmatoma of the muscles, e.g., of the sterno-elcido-mastoideus; that of the external ear, othæmatoma, especially of the insane; wounds from swallowing sharp or pointed objects; those of the skin and mucous membranes from friction, the action

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* This perverted use of the word APOPLEXY, so common in text-books and lectures, has proved most misleading to students. Previous to 1820 the word was employed, as it should be, to denominate a group of symptoms, which may be caused by many morbid conditions (not hæmorrhage alone). —[ED.]

of substances producing excoriations, etc., especially in the urinary tract (catheter, calculi), in the lower part of the intestinal canal (hard feces), in the upper part (by intestinal worms: *anchylostomum duodenale—vide* p. 124), in the genitals (subcutaneous hæmorrhages and galling from coitus—hæmatoma of the vulva from pressure of the head of the fœtus in parturition); by stretching and tearing, especially of the granular surface of ulcers, as of the lower part of the rectum, of the chapped surface of the lips and hands; in the breaking open of cancers on the surface of the skin and mucous membranes.

Through traumatic causes is explained the origin of hæmatocele from hydrocele, *hæmatoma patellare* from a hygroma, as well as the bloody mixtures in many strumous, serous, mucous and colloid cysts (so-called hæmatocystides).

Strong muscular movements, as straining at stool, sneezing, coughing, *e.g.* in whooping-cough, are often followed by rupture of vessels. Sometimes the vessels or organs were previously affected *e.g.*, strong bodily movements cause hæmaturia, during the existence of renal and vesical calculi. After general convulsions there are frequently seen in the dead body small subserous and other hæmorrhages, in tetanic spasm often hæmorrhages in the muscles; even in the skin of the face of the living after severe epileptic convulsions.

Here also belongs the influence of a decrease of atmospheric pressure, as may be seen, under cupping-glasses, Junod's boots, and sometimes in the climbing of mountains.

2. Diminished capacity of resistance of the wall of the heart and vessels, dependent upon original or acquired changes in their texture. Here belongs in the first place the long exclusion of the blood from a vascular region and the resulting softening of the vessel-wall in embolic processes, etc. (*vide* p. 203). Under this head belongs also inflammatory and gangrenous softening and fatty metamorphosis of the circulatory apparatus. Thus arise ruptures of the heart from acute and chronic myocarditis and from fatty metamorphosis of the muscular substance of the heart; ruptures of arteries of every calibre from chronic endarteritis and fatty metamorphosis of the internal and middle coats, sometimes with prior aneurismal dilatation (in the brain, in the lungs, etc.), sometimes without these (as in hæmorrhagic infarctions of the lungs in cardiac affections, etc.); ruptures of veins in parts destroyed by gangrene, etc.; rupture of the capillaries from their fatty metamorphosis. Besides, all young vessels have very delicate walls: hence the frequent hæmorrhages in the new-born; the bleedings from the quickly grown vessels in inflammation (in pachymeningitis, the cause of the intermeningeal apoplexy or of hæmatoma of the dura mater), in pleurisy, pericarditis, etc. (hæmorrhagic exudations), in retro- or peri-uterine hæmatocele, in granulations. Finally, hæmorrhages may appear from diminished capacity of resistance of the tissues surrounding the vessels, *e.g.*, of the muscles in waxy degeneration (muscle-hæmatoma in the rectus abdominis in typhoid fever), of the brain in its softening, of the thyroid gland in gelatinous goitre.

Rokitansky and Virchow have seen the vessels of young girls very small and thin-walled, and consequent repeated hæmorrhages (see Chlorosis).

Parenchymatous secondary hæmorrhages, so-called. depend partly upon the great brittleness of the granulation-vessels, partly upon extended thrombosis of the surrounding veins.

Spontaneous cerebral hæmorrhages are almost always dependent upon true aneurisms of the cerebral arteries, which aneurisms are extremely small, to the size of a

pin's head and larger (CHARCOT and BOUCHARD, *Arch. de physiol. norm. et path.*, 1868), originating in chronic arteritis. (ZENKER.)

3. INCREASED PRESSURE OF THE BLOOD WITHIN THE VESSELS IN CONSE-QUENCE OF ACTIVE OR PASSIVE HYPERÆMIA. PASSIVE hæmorrhages, *i.e.*, those dependent upon CONGESTION, are very frequent; they arise in consequence of increased lateral pressure of the blood within the veins and capillaries. The most marked example of this is found in the congestions in the region supplied by the lesser circulation from affections of the left auriculo-ventricular opening, or of the mitral valve; hence pulmonary hæmorrhages are very frequent. Here too belong the gastric and intestinal hæmorrhages in contractions of the portal vein; the same of the new-born from disturbances in the pulmonary and hepatic circulations. (*Vide* p. 186.)

The most striking example of this form of hæmorrhage is furnished by ovarian cysts, which turn upon their axis and thereby strangulate their vessels: not only the cavities of the cysts are filled with blood, but also the cavity of the peritoneum contains blood.

SPIEGELBERG (*Mon. f. Geburtsk.*, 1865, XXVI., p. 10) holds the cranial blood-tumor of the new-born to be a local manifestation of the congestions and extravasations in the child's body, dependent upon obstructions to the interchanges of gases and especially upon the premature movements of respiration. They have their origin on the cranial bones, because their diploic substance is loosely covered by periosteum, and because the vessels of the latter enter the former almost without any sheath, and thus are easily ruptured. By this is explained, how that blood effusion occurs also after relatively easy births, as well as the almost constant fluidity of the blood, at the best with small soft coagula (for it is blood which is effused in threatened or actually present asphyxia).

ACTIVE hæmorrhages occur in all grades in all forms of ACTIVE HYPER-ÆMIA, most often as nasal hæmorrhages. Upon a similar cause depends also the frequent hæmorrhages of the brain, the severe bleedings at the nose, etc., in hypertrophy of the left ventricle. (*Vide* p. 180.)

Here belong also the "cohabitation-hæmorrhages" described by WERNICH (*Berl. klin. Wschr.*, 1873, No. 9), which occur during coition, from the peculiarly constructed vascular apparatus of the uterine cervix.

Also VICARIOUS HÆMORRHAGES, especially from the nasal mucous membrane, more rarely from ulcers, etc., which sometimes regularly, sometimes irregularly occur in the absence of menstruation, are classed under this head.

Finally, from this cause arise most of the hæmorrhages which appear in the course of inflammations, as well those in common acute inflammations as of all mucous membranes, lungs and nerve centres, as the hæmorrhages in capillary and large embolisms (from endocarditis), as well as chiefly in metastatic abscesses: COLLATERAL HÆMORRHAGES.

4. CHANGES IN THE WALLS OF THE VESSELS AND IN THE BLOOD AT THE SAME TIME: HÆMORRHAGIC DIATHESIS, *i.e.*, a condition in which, in the most different localities, hæmorrhages occur without increased vascular excitement or stagnation.

The hæmorrhagic diathesis forms the chief force in true scurvy, in diseases characterized by extravasations of blood (*purpura simplex, peliosis rheumatica, morbus maculosus Werlhofii*), in the bleeding sickness (hæmophilia). It also sometimes occurs in typhoid fever, small-pox, scarlet fever, measles; seldom in all the other diseases with high temperatures, which

then are very dangerous; in some contagio-miasmatic diseases, as yellow fever, cholera, the plague; in septicæmia; in the severe forms of jaundice, dependent or not on disease of the liver; in acute poisoning by phosphorus and the mineral acids, during the extended use of mercury, in alcoholism; in many cases of Bright's disease; in many diseases of the spleen, especially leucocythæmia; sometimes in chlorosis with amenorrhœa, etc.

The immediate cause of hæmorrhage in the hæmorrhagic diathesis is still unknown. Experiments by GASPARD, STICH, VIRCHOW, O. WEBER, etc., on putrid infection of the blood, show that here true chemical substances are the causes of hæmorrhages; according to WEBER, probably sulphuretted hydrogen and sulphuret of ammonia. PRUSSAK (STRICKER, *Wiener Sitzgsb.*, 1867, LVI.) observed an abundant exit of red blood-corpuscles through the uninjured capillary-wall in frogs, perhaps also in rabbits, into which he had injected a large quantity of a solution of common salt. This was the first certain demonstration of the independence of such hæmorrhages from blood-pressure, but through blood-changes of a chemical character (or of the vessel-wall ?). COHNHEIM (*Die embol. Proc.*, 1872, p. 26) could not verify these experiments. See several cases reported by the author (*Arch. d. Heilk.*, 1869, X., p. 327). (See also the so-called acute fatty-degeneration.)

A hæmorrhagic diathesis may have its origin in a long use of the mineral acids. The effect of iodine in some individuals is peculiar, in that it gives rise sometimes to exanthemata, sometimes to hæmorrhages.

In a case of *purpura simplex*, GRIESINGER found in places where tightly bound garters had exercised a pressure, almost no purpura spots, and founded thereon a therapeusis consisting in bandaging, etc. (*Arch. d. Heilk.*, IV., p. 383).

HÆMORRHAGES are not infrequently DEPENDENT UPON THE SIMULTANEOUS ACTION OF TWO OR MORE OF THE CAUSES NAMED. Thus, *e.g.*, bronchial hæmorrhages from changes in the vessel-wall and from dilatation of the vessels actively or passively (congestions from tubercular deposits, etc.).

Many organs exhibit a stronger PREDISPOSITION TO HÆMORRHAGES than others, because of the pliability of the surrounding parts; *e.g.*, many parts of the subcutaneous cellular tissue, of the submucous tissue. The same is true of the brain, lungs, spleen, in which organs every intense inflammation is followed by very numerous extravasations: red softening of the brain, red hepatization of the lungs, owe color and name to this predisposition. Other parts frequently become the seat of hæmorrhages, only because they are more exposed to injurious influences, as the nasal mucous membrane (mechanical influences, more frequently changes in atmospheric temperature), that of the rectum (mechanical influences), that of the conjunctiva, etc.

Since the causes mentioned belong unequally to various ages, the old opinion can rightly be maintained, that the head in children, the thorax in youth, the abdomen in later age, most frequently furnish the causes for hemorrhages.

THE ANATOMICAL CHANGES IN THE BLEEDING VESSELS THEMSELVES, AS WELL AS OF THE TISSUES AND ORGANS AT THE SEAT OF HÆMORRHAGE, differ, especially with the character of the bleeding vessels, with the size of the hæmorrhage, with the time since which it occurred, and with the kind of tissue and organ which is the seat of the hæmorrhage.

That which first of all concerns the BLEEDING VESSELS THEMSELVES is that THE GREATER NUMBER OF HÆMORRHAGES CEASE OF THEMSELVES. The chief causes of this SPONTANEOUS BLOOD-ARREST are, first of all, COAGULATION OF THE BLOOD, which appears as soon as the blood leaves the vessels. The influence of the connective tissue, especially of young new-formations; the presence of foreign bodies, among which blood-coagula also belongs; the

action of certain secretions (synovia, saliva), and of pus, hastens coagula-
tion. Besides, the SPONTANEOUS RETRACTION AND CONTRACTION OF THE
VESSELS, which appears in the smaller arteries rich in muscular tissue,
longitudinal and transverse, and is a consequence partly of the removal of
tension, partly of the traumatic irritation; the resulting fine plaiting of the
inner surface increases the points of deposit for blood-coagulation. THE
SURROUNDING TISSUES, at first by their serous or cellular infiltration, later
by their contraction, cause closure of the bleeding vessels, and thus an
arrest of the blood, especially if they, like the skin, scrotal sac, labia, mam-
mæ, uterus, are rich in contractile tissue, especially in organic muscles;
while rigid tissues, like spongy bones, tightly stretched fasciæ, etc., favor
the continuation of hæmorrhage. The DECREASE OF BLOOD-PRESSURE in
great losses of blood increases the absorption, causes a quicker influx of
lymph through the thoracic duct, and thereby a more abundant en-
trance of colorless blood-corpuscles into the blood, and assists also in increas-
ing the coagulability of the blood. Finally, repeated hæmorrhages heighten
the coagulability of the blood: in hæmorrhages the last portions of blood
coagulate almost instantaneously after the flow.

SOME CIRCUMSTANCES PREVENT OR RENDER DIFFICULT THE STOPPING OF
THE BLOOD'S FLOW. Thus longitudinal wounds and incomplete transverse
wounds of the vessels, because the contraction of the muscles only dilates
the wounds, and retraction of the vessel is rendered impossible. Hæmor-
rhages in parts which are dependent cease with greater difficulty than in
those otherwise situated (hæmorrhages of the legs, rectum); strong mus-
cular movements promote bleeding (known means of assistance in venesec-
tion). In like manner pressure acts upon one or more of the veins belong-
ing to the same vascular region; also violent expiratory acts, especially in
crying, coughing, sneezing. Likewise warmth exerts an influence, in that
it relaxes the vessels.

The FINAL CLOSURE OF BLEEDING VESSELS follows upon the formation of a
coagulum, which fills the wounded vessel as far as the nearest collateral
branch, and which, within a few weeks, grows pale, becomes firmer, and is
intimately attached to the vessel-wall: it ORGANIZES. This takes place in
the same way as in thrombosis of another kind (see p. 191). Connective
tissue-fibres and vessels are formed, which first appear in communication
with the vessel's wall, later with the channel of the wounded vessel.

The MANNER OF HEALING OF BLEEDING PARTS OF THE CIRCULATORY SYSTEM is
of high theoretical and especially of practical interest. HÆMORRHAGES FROM THE
HEART, GREAT ARTERIES, and great veins are mostly followed by very quick death:
in very rare cases a permanent cure takes place after small ruptures of the heart in
adhesive pericarditis, and in laceration of the internal and middle coats of the aorta,
with effusion of blood under the adventitia. Healing of the WOUNDS OF THE RE-
MAINING ARTERIES differs with the size of the artery, and with size and character of the
wound. After complete section or laceration of small or medium sized arteries in a
healthy state, the middle coat which is firmly connected with the inner coat, strongly
contracts transversely, and recedes within the external coat, with which it is loosely
connected; a thrombus forms between the point of severance and the nearest branch
above or below, which thrombus adheres to the vessel wall, and in the course of time
continues to shrink. Completely severed arteries of large size likewise contract, but
for the most part not so completely that the hæmorrhage is arrested; this happens
sometimes, at least temporarily, from a weakness of the heart's contractions through
loss of blood, and even faintness. Wounds of arteries which do not affect their whole
circumference, differ in their effects with the size of wounds. Small penetrating
wounds mostly give rise to small thrombosis at the point of injury, as well as in the
tissue immediately surrounding it, and thereby healing. Large wounds which affect
only a part of the vessel, cause a strong transverse and longitudinal contraction of

the walls, especially of the middle coat, which enlarges the wound, and which finally can heal only through the formation of a thrombosis of the surrounding tissue, and of the artery itself as far as the next collateral branch. HÆMORRHAGES FROM SMALL VEINS, AND FROM THOSE OF MEDIUM SIZE usually cease through collapse of the central and peripheral extremities of the veins, after coagulation of the blood as far as the nearest valve, or the nearest collateral branch, and through the adhesion of the venous walls; pressure of the surrounding parts assists in the arrest, except when the latter are inflexible or indurated. HÆMORRHAGES FROM THE CAPILLARIES are controlled partly through coagulation of the blood, partly by pressure through con-traction of the surrounding parts.

Consult also BIESIADECKI (*Tagebl. d. Naturf.- Vers.*, 1872, p. 217).

ᐟ The healing of wounds of vessels is of especial surgical interest in LIGATURE OF VESSELS. AT THE POINT OF LIGATURE there occurs a suppurative dissolution or necrosis of the adventitia (the internal and middle coats are cut through by the ligature and retract), and eventually a simultaneous solution of the surrounding tissues: then the ligature falls off. This takes place, according to the size of the vessel, in from three to twenty-six days. It occurs too early, if before the thrombus has become organized and shrinks, as in diseased arteries, or if suppuration even appears in the thrombus, or if the thrombus is too short (if large branches are given off immediately above the point at which the ligature was applied) ; thus giving rise to so-called SECONDARY HÆMORRHAGE.

KLEBS describes as septic, or tertiary hæmorrhages those dependent on the penetra-tion of his *microsporon* into the arteries or veins. (*Vide* PYÆMIA.)

The fate of the ligature after ligation of the arteries in their continuity is essen-tially the same as after ligation of their divided extremity, as in amputations; except that a coagulum is formed as far as the nearest collateral branch above and below the ligature. Immediately thereafter the vessels above and below the ligated artery dilate and introduce the COLLATERAL CIRCULATION. This is followed, always in the small arteries, almost always in those of medium size, and often even in those of large size (carotid, crural, subclavian), by a sufficient supply of blood to the part beyond ; the temperature of the part remains normal, or is lowered for a few hours only; all the functions remain unaffected. Proportionately rare are disturbances arising from : ischæmia, when the collateral circulation is only incompletely formed ; sometimes venous congestions, in consequence of lessened *vis a tergo ;* sometimes collateral hyperæmiæ, when the collateral circulation has been established too quickly and too freely.

The rapidity of the formation of the collateral circulation after ligation of arteries in their continuity, is shown by the following results from experiments made in a large fleshy dog by O. WEBER :

Blood-pressure of crural in free circulation.....................62–75 mm.
    "   "   "   after ligation at central end............72–85 "
    "   "   "   "   " periph. end immediately.30–33 "
                           One-half hour later...to 44 "

RECENT HÆMORRHAGES INTO TISSUES behave in accordance with the size of the hæmorrhage, the kind of tissue involved, etc.

If the HÆMORRHAGES ARE VERY SMALL, numerous red and isolated white blood-corpuscles, alone or at the same time with fibrin in molecular or reticulated form, are found in the tissues either within the natural spaces of the connective-tissue, especially also in the radicles of the lymphatics, or between the separated elements of the tissue (epithelial cells, gland-cells, connective-tissue bundles). In these cases the blood-corpuscles, at least the red, may penetrate into the interior of cells, whence the CELLS CONTAINING BLOOD-CORPUSCLES arise, as well from the contractile cells of connective tissue, etc., as from epithelial (oral cavity, œsophagus, bladder, intestines, lungs), from glandular cells (spleen, liver), from cellular new-formations (carcinoma). It is hardly possible to draw the line between normal and pathological cells containing blood-corpuscles : in the spleen, bone-marrow, ependyma of the cerebral ventricles, their occurrence is as frequent as their absence.

The author (*Arch. d. Heilk.*, 1868, IX., p. 497; 1869, X., p. 337) has accurately

described many forms of such small, epithelial hæmorrhages in man. See also the chapter on pigment-metamorphosis.

When the HÆMORRHAGES ARE LARGER and affect soft tissues, the elements of the latter are then often SEPARATED FROM ONE ANOTHER: a hæmorrhage under the surface, especially of cuticular organs, is called hæmatoma or blood-boil; one into the interior, especially of parenchymatous organs, either simple hæmorrhage (as into the intermediate space of torn muscles, broken bones) or hæmorrhagic infarction. Or the tissues, especially in arterial hæmorrhages, are TORN: hæmorrhagic focus, clot.

HÆMATOMA, BLOOD-TUMOR or BLOOD-BOIL, forms a tumor-shaped, sometimes more globular, sometimes flatter accumulation of extravasated fluid or coagulated blood, and of various sizes, which arises from different causes (congestions, etc.), and most often occupies the surface of extended organs. Here belong: the blood-vesicles of the skin, which arise on the fingers from bruising, and lie in the so-called stratum lucidum; similar hæmorrhages there, or in the stratified epithelium of the mucous membranes in *morbus maculosus*, etc.; besides, the so-called blood-boils in the subcutaneous connective tissue, hæmatoma of the vulva in the tissues of the labia, polypoid hæmatoma of the uterus at the point of insertion of the placenta, cephalo-hæmatoma between the cranial bones and pericranium, othæmatoma between the aural cartilages and perichondrium, hæmatoma of the dura mater between the newly-formed layers on its inner surface. To hæmatomata belong also the false or traumatic aneurisms: hæmatomata are distinguished as diffuse, and as encapsuled or circumscribed.

The origin of OTHÆMATOMA is easily explained, according to L. MEYER (*Med. Ctrlbl.*, 1864, No. 55), by the fact that the reticular cartilage of the ear, in all ages, always contains vessels. Others, especially GUDDEN (*Virch. Arch.*, LI., p. 457), dispute this. FLESH-MOLES, so-called, arise from numerous effusions of blood into the tissue of the placenta. HÆMATOMATA OF THE PLACENTA all proceed, according to GIERSE and H MECKEL, from blood-coagula. The youngest hæmatomata appear to arise only in the uterine portions of the placenta. According to KLEBS the effusion of blood at first takes place only in the lymph-spaces of the placenta.

HÆMORRHAGIC INFARCTIONS form a rounded or wedge-shaped, not tumor-shaped, central or peripheral, circumscribed, dark or black red, dense masses of effused blood, which are of different sizes, and on section present a uniform or granular appearance. Under the microscope blood-corpuscles and fibrin are found, not only in the normal cavities of the organ (alveoli of the lungs, urinary canal, etc.), but also between the tissue-elements; the latter are usually not at all torn or only partly so, for the most part merely separated from one another. (See also p. 217.)

HÆMORRHAGIC FOCI show a portion of varying size of a tissue or organ, oftenest the brain, torn and blood effused into the rent; the blood is seldom fluid, mostly coagulated and peripherically containing fragments of tissue. In rare cases the fibrin coagulates in the periphery, and forms a kind of capsule around the remaining part of the extravasation.

These all (hæmorrhagic infarction, etc.) merge into one another.

The TISSUES IN THE VICINITY of recent hæmorrhages are seldom normal, mostly reddish or yellowish through diffusion of the coloring matter of the blood, or through filling of the lymphatics with blood, or through true hyperæmia; frequently they are also œdematous. The surrounding tissues are even compressed in greater extravasations, as in closed cavities, sometimes in greater extension.

In all these cases the torn vessel itself is almost never found. It is most frequently found when vessels of medium size, or aneurisms of small vessels burst, in capillary cerebral hæmorrhages, when the small white points in the centre of the extravasation are the torn (arterial) vessels.

When a HÆMORRHAGE INTO A TISSUE has taken place, in organs rich in lymphatic vessels, a part of the blood, which at the time of the hæmorrhage was forced into these vessels, is driven still farther on—a process which in the lungs and kidneys it is easy to observe. In very small hæmorrhages, as in those *per diapedesin*, etc., all the extravasated blood-corpuscles may in this manner be removed. In the remaining cases, however, all or nearly all the blood remains, and here becomes farther changed.

ORTH (*Virch. Arch.*, 1872, LVI., p. 269) found in a case of traumatic hæmorrhage of the lower extremity an inguinal gland of the size of a plum, dark red, fixed ; its lymph-vessels were filled with blood-corpuscles, as well as the glandular parenchyma, the lymph-corpuscles of which were entirely wanting.

The CHANGES WHICH EXTRAVASATED BLOOD UNDERGOES are: most frequently RESORPTION, at first of the serum, then of the remaining constituents. The latter are seldom absorbed before the appearance of coagulation, as in cephalæmatoma of the new-born, etc. Resorption appears mostly only after coagulation. This becomes possible by simple solution of the fibrin and transformation of the white blood-corpuscles into albuminous and fatty detritus. To this perhaps also is added a serous exudation from the surrounding vessels. Resorption of the red blood-corpuscles, according to some, is accomplished by their entrance *in toto* into the interior of surrounding cells, and there undergoing farther change ; according to others, on the other hand, by the transformation of their pigment at the place of extravasation into granular or crystalline hæmatoidin (*vide* Pigmentary Metamorphosis). In most of the larger hæmorrhages with more or less laceration of the tissues, a complete restitution of the latter never takes place.

A DRYING-UP and final wearing off of the bloody effusion occurs in small hæmatomata, which occupy the epithelial layers of the skin (blood-blisters) or mucous membranes provided with laminated epithelium (œsophagus, bladder).

A CHEESY METAMORPHOSIS of the blood-coagulum occurs sometimes in the interior of normal tissues, especially of the lungs and spleen, as well as within large vascular new-formations (many cancers, especially of the kidneys).

More rarely there occurs CALCIFICATION, as well as AMYLOID DEGENERATION of the coagulum.

Only rarely it SOFTENS, sometimes with consecutive suppuration. This happens in large open wounds of the surface, also (after considerable bruises) in the interior especially of the extremities, rarely in the cavities of the joints, in mucous membranes, and lung-tissues.

Many cases of so-called brown softening of the œsophagus and stomach are dependent upon hæmorrhagic infarction with consecutive solution by the contents of the stomach (AUTHOR, *Arch. d. Heilk.*, 1867, VIII., p. 464. HOFFMANN, *Virch. Arch.* 1868, XLIV., p. 352).

Sometimes the effused blood becomes PUTRID in consequence of the contact of air, in hæmorrhages of the surface of the body and of the lungs, or from contact with the secretions (urine, fæces). Similar changes may then

extend to the surrounding tissues and become the causes of gangrene or of septicæmia.

Should life continue for weeks and longer after the occurrence of extravasation, still farther transformations appear in the latter itself, and in the tissues immediately adjacent to it. These changes consist in the ORGANIZATION of the effused blood, and in an analogous tissue-formation in the surrounding parts. Examples of this are furnished by tissues of almost every kind, especially the subcutaneous cellular tissue, muscles, bones, lungs, brain. Organization of the whole mass of effused blood is comparatively rare, and has been recognized with certainty in only a few places: in tenotomy, in cuts and bruises of the muscles, in fibrous polypi of the uterus, in many cerebral hæmorrhages connective tissue thus has its origin, while in fracture of bones, in cephalæmatoma, etc., osseous tissue is formed. Much more frequently the periphery only of the effused blood is organized, while its central portion liquefies and is wholly or partially absorbed: apoplectic cysts and indurations. Not infrequently the tissues in immediate contact with the extravasation in part maintain their integrity and become in part absorbed, so that generally a regularly rounded space is formed, the inner surface of which becomes, through the organization above-mentioned, smooth and dense: so-called APOPLECTIC CYST. This is filled at first with a pultaceous mass, later with serum. Its internal surface is often of a yellow color from pigment-change, red or blackish, but always without epithelial lining. Cysts of this kind almost always continue to exist. APOPLECTIC CICATRICES have for the most part an immediate origin, rarely after previous formation of cysts. These cicatrices represent an irregularly shaped fissure, whose walls are indurated and are in immediate contact with one another, or are separated by pigment.

THE CHANGES WHICH APPEAR IN TISSUES SURROUNDING OLD HÆMORRHAGIC COLLECTIONS are, besides the pigmentation, connective tissue or osseous new-formations, and the anæmia and hyperæmia already mentioned: inflammation, suppuration (*abscès hématiques*), gangrene, atrophy of essential tissue-elements.

HÆMORRHAGES INTO PRE-EXISTING CAVITIES AND CANALS behave in a quite simple manner.

In hæmorrhages into SEROUS CAVITIES the blood is not rarely entirely absorbed: thus in traumatic hæmatothorax, hæmatocele. Otherwise the above-mentioned metamorphoses set in, especially pigmentary metamorphosis of the corpuscles, and drying or softening of the fibrin. Larger hæmorrhages are sometimes followed by suppurative inflammation. The blood freely effused into the pelvic cavity in peri- or retro-uterine hæmatocele is reabsorbed, or encapsuled through a reactive peritonitis, or it suppurates.

The blood effused upon MUCOUS MEMBRANES does not long remain where extravasated, but is removed in various ways. The mucous membrane itself often shows no changes worthy of notice. Here it is to be observed that the point at which, in the dead body, the blood is found does not always correspond with the proper seat of the hæmorrhage: in gastric hæmorrhages the stomach is sometimes empty, while the small and large intestines contain blood in large quantity; in hæmorrhages from one lung blood is not infrequently found in the bronchi and alveoli of this, as well as in those of the other lung, or blood in the stomach, etc. But if the blood is not removed, it suffers the same changes, as in parenchyma, and serous cavities. Especially important in this connection are the hæmorrhages from the bronchi and bronchiectases in other normal bronchi and alveoli of the same lobe or of that of the other lung: the removal of the

blood being prevented by various circumstances, the blood here dries up and deprives the parts of air, but gives rise also to new catarrhs and infiltrations; or it putrefies, as in ulcerous bronchiectasis, and may thus be followed by gangrene of the surrounding tissue.

PERL and LIPMANN (*Virch. Arch.*, LI., p. 552) found in artificial pulmonary hæmorrhages of rabbits and dogs, that the blood effused in a bronchial hæmorrhage passed into the finest bronchi and into the alveoli, that after 12 hours coagula are no longer demonstrable in the larger bronchi, that the blood effused into the previously sound air-passages does not act as excitants of inflammation, but is gradually resorbed without leaving behind any lung-changes other than moderate emphysema.

SOMMERBRODT (*Med. Ctrlbl.*, 1871, No. 43) injected the air-passages of dogs with blood and a solution of the sesquichloride of iron and killed them from 1–12 hours to 2–12 days thereafter. The blood which reached the alveoli induced constant catarrhal pneumonia. After 4–6, but especially after 24 hours, the characteristic large cells (COLBERG) appear with the blood-cells, and are on the 4–5 day present in enormous quantities. The cells have their origin in the epithelia of the alveoli; these increase in size, become turbid, and are distinguished by leaving behind of open spaces in the epithelial surface. The great cells take up into themselves red blood-cells, sometimes 3 to 5. On the 11th and 12th day the great cells are colored brown, and equal those observed in affections of the heart.

The blood which has passed from bronchiectases or other forms of caverns into other parts of the lung, I found in a few cases quite wanting in fibrin.

That blood, which is freely effused into cavities and remains for a longer time, finally organizes, has long been maintained with respect to the bloody or fibrinous polypi (polypoid hæmatoma) of the uterus. This polypus is always a product of pregnancy. Either the retained membranes of an abortive or retained placenta furnish the stem on to which the blood-mass still farther collects and coagulates, or they arise after complete separation of the after birth, through opposition of the fibrinous coagula to the protruding thrombi of the part where the placenta was inserted, which latter sometimes, during an otherwise tolerable involution of the uterus, protruded as a round tumor into the uterine cavity. (KIWISCH, SCANZONI, VIRCHOW, ROKITANSKY, KLOB, FRÄNKEL.)

Hæmorrhages into the larger GLAND-DUCTS act in general like those on mucous membranes; those into the smaller, *e.g.*, sweat-glands, distend them and cause small tumors similar to hæmatomata.

SYMPTOMS AND CONSEQUENCES OF HÆMORRHAGES.

The symptoms of hæmorrhage depend partly upon the kind of hæmorrhage, partly on its size, partly on its location, partly on the changes within the extravasation.

EXTERNAL HÆMORRHAGES are easily recognized. In wounds of external parts (of the body and of the extremities) the blood flows, with the exception of rare cases (*aneurisma spurium* and *a. varicosum*) immediately to the surface. From the mucous membranes, out of the glands and ducts, the blood, wholly or in part, flows immediately to the exterior, *e.g.*, from the nose, mouth, vagina, urethra. Or, the effused blood itself by irritation induces acts which remove the blood: bloody expectoration, bloody vomiting, bloody urination, bloody uterine flow, bloody stools.

The blood of hæmorrhage is either PURE; or it is MIXED with the contents of the channels through which it passes to the exterior, with excrement, urine, mucus, gastric juice, air. In general it is cleaner the nearer the hæmorrhage is to the opening of the cavities. By the urine it becomes very dilute, especially if it is already mixed with it in the kidneys; by the gastric juice it is colored brownish or black; by the vaginal secretion, its coagulation is prevented. Rarely does it come to the exterior in a fluid state, but mostly coagulated, in large lumps, or (in the intestine) in crum-

bling masses, or in peculiar shapes corresponding to the locality of the
hæmorrhage (*e.g.*, uterus, ureters).

The CHARACTER OF THE HÆMORRHAGE, *i.e.*, THE QUESTION WHETHER A
HÆMORRHAGE PROCEEDS FROM AN ARTERY OR VEIN OR FROM THE CAPILLARIES,
is, in many cases even of external hæmorrhages, with difficulty and some-
times not at all to be determined. As to whether an artery or vein is
the cause of a hæmorrhage, the following are, with respect to fresh EXTER-
NAL INJURIES, some of the considerations: the anatomical position of the
vessels; the thickness of the vessel-wall (but arteries are on account of the
anomalies of their course not always equally thick; the wall of veins may be
thickened by chronic inflammation); the color of the blood (but in deep nar-
cosis from chloroform arterial blood resembles venous blood; in the simul-
taneous wounding of neighboring arteries and veins both kinds of blood are
mixed); the nature of the blood-stream; in wounds of large arteries and those
of medium size the stream increases correspondingly with the heart's impulse
and especially with expiration, while in small arteries it is quite regular; the
blood flows from the veins in a tolerably regular stream, in the cervical
veins more strongly during expiration (but in high fevers, as well as when
the veins at the point of injury are immediately bound to an artery, the
venous stream also shows, of course weak, pulsation. In deep, narrow
wounds, however, all the above mentioned characters, as well as the direction
of the wound, are not to be depended upon. To establish the diagnosis
compression of the larger vessels immediately above the wound is employed;
generally, hæmorrhage from an artery thereby ceases, while that from a
vein is by the same means increased. Also, the quantity of blood lost
during a given time is much greater from an artery than from a vein. In
PARENCHYMATOUS HÆMORRHAGES a great quantity of mixed blood, *i.e.*, of
arterial and venous blood, is poured out in a comparatively short time;
the blood streams forth from numberless openings as from a sponge or
watering spout. They occur as well in normal tissues (corpora cavernosa,
spongy bones, eyelids, tongue, after cuts, lacerations and bruises), as in new-
formations (vascular tumors, vascular sarcomata and cancers, fungous gran-
ulations). In CAPILLARY HÆMORRHAGES the quantity of dark blood effused
is comparatively scanty.

Hæmorrhages into the tissue of FLAT ORGANS are to be recognized only upon
the skin and the neighboring mucous membranes (conjunctiva, nose, mouth,
pharynx, etc.), the blood appears through the surface with a bright or dark-
red color, according to the quantity of the extravasation. The skin or
mucous membrane is not thereby raised; or it forms a diffuse or circum-
scribed tumor (hæmatoma). Larger hæmorrhages under the periosteum de-
termine an insufficient nourishment of the surface of bones. Larger
hæmorrhages into the *decidua serotina* are always followed by abortion,
etc.

In INTERNAL HÆMORRHAGES the question from which kind of vessels the
blood flows is usually of little consequence. The color of arterial blood is
bright red, of venous blood dark red; but arterial blood stagnant in the
body, as well as the blood in asphyxia, in deep chloroform narcosis, soon
becomes dark red; venous blood becomes bright red in the air, and so the
color cannot be relied on. Besides, most hæmorrhages are not of one pure
kind of blood, but, since they often proceed from the capillaries of the
parenchyma, are mixed. The blood coming from the air-passages and lungs
possesses an alkaline reaction, that from the stomach an acid one.

Sometimes the cavity into which the hæmorrhage occurs becomes dis-

tended, to a greater or less extent, by the accumulation of blood, as most frequently happens in the uterus, stomach, and bladder.

Disorders of function may arise from obstructions of canals; anuria from obstruction of the urethra; dyspnœa from obstruction of the larynx and drawing of blood during inspiration into the fine bronchi and alveoli of the lung, etc. Those hæmorrhages more rarely remain latent, in which the blood accumulates in quantities in the cavities above mentioned (stomach, uterus). Small effusions of blood are then altogether latent; the large are recognizable only from their consequent disorders of function (nausea, vomiting, etc.).

Like external hæmorrhages, the internal ones, the blood of which flows to the exterior, are of interest only with respect to the quantity of blood lost.

Hæmorrhages into parenchymata are altogether more dangerous than those upon free surfaces, because in the former the blood prevented from flowing away exerts its influence by pressure, etc.; hæmorrhages into the parenchyma, which cannot extend, or only to a slightly, as in the brain and spinal cord, are more dangerous and have more symptoms than those into organs where extension is possible, as into the lungs, liver, and spleen. Hæmorrhages into the brain and spinal cord give rise to symptoms which differ with the site of the hæmorrhage (walls of the lateral ventricles, centre of the pons, cortical substance, etc.); therefrom frequently result paralyses of muscles, paralyses of sensation, etc.

The degree of danger to the whole organism is in great part dependent upon the quantity of blood poured out, which is sometimes very small, sometimes reaches many pounds, and upon the time in which the single or repeated hæmorrhages takes place. Hæmorrhage is followed by a sudden or very quick death (rupture of the heart, of large aneurisms, etc.) in adults when as much as five pounds of blood, in the new-born when a few ounces have been lost. Or, paleness of the skin and visible mucous membranes, pointing of the nose, weakness, feeble voice, small soft pulse, nausea, cold sweat, dusky complexion, vertigo, shaking or convulsions, fainting, are the immediate symptoms which, within a few hours, are followed by death (external hæmorrhages, hæmorrhages in the puerperal state, gastric and intestinal hæmorrhages, etc.), or in comparatively rare cases by recovery. Fainting appears in adults when the loss of blood occurs suddenly or quickly, and to the amount of about one pound. Long continuing, or frequently returning small hæmorrhages, besides causing the last-named symptoms, especially fainting, give rise to hydræmia and dropsy (bleeding from the nose, from the female genitals, urinary bladder, rectum, etc., especially in cancer of these parts; hæmorrhages into various tissues in scorbutus, etc.; intestinal hæmorrhages from the *anchylostomum duodenale*). Internal hæmorrhages of considerable amount are usually to be diagnosed from the symptoms mentioned. (*vide* General Anæmia.)

A favorable influence is often exercised on existing orgasm by small or moderately large local hæmorrhages: thus bleeding at the nose, in hyperæmia of the head, besides in many febrile diseases; or in congestions: thus the hæmorrhoidal bleedings. In general, also, the effect of vicarious hæmorrhages is usually favorable, *e.g.*, from the nose, from an ulcer on the foot in delayed menstruation.

The diagnosis of hæmorrhage is in most cases, when the blood does not appear to view, as, *e. g.*, in hæmorrhagic infarctions of the lungs, very difficult to establish, or it is impossible, except when a very large extravasation occurs in a very short

time. The quickness of the appearance of the symptoms, the preceding and present morbid conditions of other organs (heart, vessels), the influence upon the general state (anæmia, etc.), must enter into the formation of the diagnosis.

The DIAGNOSIS OF EXTERNAL HÆMORRHAGE is frequently not to be made with safety without the assistance of microscopical or chemical methods of examination, especially since the blood is often mixed with other substances, and since, besides, the sick are affected by illusions, or practice intended simulation.

If the substance for examination be fluid, preferably a part from the territory of the vessel involved, it should be subjected to MICROSCOPICAL EXAMINATION. If it be dry or fixed (blood stains), it should be brought in contact with one or two drops of water for a quarter to a half hour. Then red and colorless blood-globules and coagulated fibrin are to be sought for. The red corpuscles do not, for the most part, long retain their condition in liquids not alkaline. In the dried state they are easily lost in soaking the blood spots, but again appear in concentrated alkaline solutions. To look for colorless blood-corpuscles and fibrinous coagula in the examination of the liquids in question, is mostly of no moment, but in blood-stains it is of the highest value.

Only when microscopical examination does not or not clearly demonstrate blood-corpuscles, are CHEMICAL processes to be resorted to. If the mass in question contains an abundance of fat, the latter is separated by alcohol or ether. Then the mass is heated, whereby the albuminous substances, almost always at the same time present, are coagulated, and at the same time separated with the hæmatin. The dried residue is treated with alcohol containing a few drops of sulphuric or muriatic acid. If hæmatin be present, the solution will be reddish, and after evaporation will leave behind a brownish mass. This is soluble in caustic potassa and carbonate of potash, soda and ammonia; insoluble in weak acids, and after incineration furnishes a brownish-yellow ash, rich in iron. Or, a small part of the substance should be boiled from one-half to one minute, with three to ten times its quantity of acetic acid, and enough common salt to cover the point of a small knife. At first the liquid is colored a dark gray, and appears muddy; but soon it becomes clear, and lets fall a very small quantity of insoluble substance (hæmin). This under the microscope appears as dark-brown or black rhombic tables (HÆMIN CRYSTALS), which are not affected, or very little, by the different reagents.

Whether the blood is human, or belongs to other mammals, cannot be determined. When red blood-corpuscles of oval form are found, as, e.g., in many simulated cases of bloody expectoration and vomiting, they are known as belonging to the blood of birds, or amphibia.

APPENDIX.

LYMPHORRHAGIA.

LYMPHORRHAGIA is a term used to express the flow of lymph out of its natural channels, the lymphatic vessels, on account of wounds or diseases of those vessels. The extravasated lymph flows either into the surrounding tissues, or upon a free surface. The latter occurs either outward (lymph-fistulæ) or into internal canals. In this manner is formed CHYLOUS URINE, which results from an effusion of lymph into the urinary tracts.

The farther consideration of this subject belongs to special pathology. With respect to chylous urine, consult especially GUBLER and CARTER. In a case observed by myself there was, from time to time, besides chylous urine, an evacuation of coagula as long and as thick as the finger, consisting exclusively of fibrin and colorless corpuscles.

5. DROPSY.

(ŒDEMA AND ANASARCA.)

LOWER, *Tract. de corde*, 1669.—WILLIS, *Opera omnia*, 1681.—HALES. *Statik des Geblüts*, 1748.—BOUILLAUD, *Journ. de physiol.*, 1823, III., p. 89.—BRIGHT, *Rep. on*

Med. Cases, 1827; *Guy's Hosp. Rep.*, 1836.—MAGENDIE, *Leç. sur les phenom. phys. de la vie*, 1837.—HENLE, *Hufel. Journ.*, 1840; *Ztschr. f. rat. Med.*, 1844, I.; *Hdb. d. rat. Path.*, II.—VIRCHOW, *Virch. Arch.*, 1847, I., p. 572; *Handb. d. spec. Path. u. Ther.*, 1854, I., pp. 46 *et* 182.—C. SCHMIDT, *Ann. d Chemie*, 1848, LXVI., p. 342; *Characteristik d. epid. Cholera*, 1850, p. 140.—BERNARD, *Compt. rend. de la soc. de biol.*, 1849, I.—ABEILLE, *Traité des hydropsies et des cystes*, 1852.—BECQUEREL et RODIER, *Gaz. méd.*, 1852.—MIALHE, *Union méd.*, 1852.—HOPPE, *Virch. Arch.*, 1856, IX., p 245, XVI., p. 391.—A. SCHMIDT, *Arch. f. Anat., Phys.*, etc., 1861, pp. 545 et 675; 1862, pp. 428 et 533.—TOMSA, *Sitzber. d. Wien. Acad.*, 1862, p. 185.—LUDWIG, *Oesterr. Jahrb.*, 1863, p. 35.—O. WEBER, *Hdb. d. Chir.*, 1865, I., p. 192.

DROPSY is the morbid accumulation of a fluid more or less like the blood-serum and lymph in the parenchyma of the tissues and organs, or in closed serous cavities. It is dependent chiefly on disorders of the circulation.

If dropsy affect the parenchyma, it is called: ŒDEMA (œdematous or dropsical infiltration), ANASARCA or hyposarca, *aqua intercus*. If it affect closed cavities: DROPSY, free dropsy, hydropsy, dropsy of cavities, and receives special names from the cavities affected: hydro-peritoneum, ascites simply, abdominal dropsy; hydro-thorax, dropsy of the thoracic cavity; hydro-pericardium, dropsy of the pericardium; *hydrocephalus externus* and *h. internus, h. centralis, hydrops ventriculorum*, external and internal dropsy of the head; hydrocele, dropsy of the scrotum; hydrarthrosis, dropsy of the joints; hydrophthalmus, dropsy of the eye.

Contrary to the usual custom of speaking, liquid effusion into the cavities of the alveoli of the lungs is traditionally termed pulmonary œdema. Œdema of the glottis, so-called, is more rarely an œdematous, more frequently a sero-purulent infiltration; it does not affect the glottis, but the folds of mucous membrane at the entrance to the larynx.

Dropsy is either LOCAL (dropsy of any cavity, œdema of an extremity), or it affects more or less THE WHOLE BODY (general dropsy).

ŒDEMA * consists in a PATHOLOGICAL ACCUMULATION of quantitatively and qualitatively changed lymph in the lymphatic radicles, also in other spaces within the tissues and within many cellular and fibrous elements. This is proven by experiment, as well as in part by pathologico-anatomical examinations, and in most cases by the ætiology.

EXPERIMENT demonstrates that transitions occur between the usual condition of tissues and œdema. Also that in animals by constricting the lips, etc., œdema can be produced and the liquid be removed by the lymphatics.

The existence of spaces between tissue-elements filled with a varying quantity of liquid, furnishes the ground of explanation not merely of the so-called tonus of tissues free from muscles, but also of the slight, scarcely recognizable degrees of œdema: puffiness of the face after night-watching, etc.

In the living animal œdema passes away by the lymphatics. If a ligature be applied to the upper lip of a dog, the lip will become very œdematous; if the ligature be removed the lymph will flow very abundantly from the opened cervical vessels, while the œdema visibly disappears. If the lip be pressed between the fin-

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* The three terms DROPSY, ANASARCA, and ŒDEMA are used in French, English, and American books in a somewhat simpler and more definite manner than in the text. Dropsy is the generic term; anasarca is a generalized dropsy; œdema a local dropsy.—[ED.]

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gers, the disappearance of the œdema and the lymph-current will be simultaneously accelerated.

Consult the experiments relative to this subject by LUDWIG and his pupils.

The unequal disposition of different parts to œdema depends partly on the difference in circumstances which affect the passage of the lymph from out of the radicles into the main branches. This latter is dependent upon the elasticity of the walls of the lymph-spaces, their muscular character and the degree of filling of the cells and glands bordering upon them; and too upon the resistances which the lymph meets with, thus upon the dimensions of the apertures, the height of the column of lymph, and the glands to be traversed. The skin of the face is acted upon by muscles, and from it the lymph flows downward; the skin of the lower extremities is provided with few muscles, and the lymph must flow upward and through many glands. (LUDWIG.)

PATHOLOGICO-ANATOMICAL INVESTIGATIONS likewise prove the above-mentioned connection between œdema and the arrest of the lymph-flow. ŒDEMATOUS INFILTRATION affects preferably the connective tissue, earliest and most strongly the areolar tissue (between vessels, muscles, intestines), the subcutaneous connective tissue, the submucous tissue, especially that of the ankles, eyelids, male genitals, under certain circumstances also that of the uvula, of the aryteno-epiglottic ligaments, etc.; later it affects the firm connective tissue and parts consisting of it, e.g., the piamater of the brain and spinal cord, and mucous membranes; farther on, smooth and striated muscles, nerve-tissue, especially the brain, glandular organs, as the lymphatic glands, liver, kidneys. Œdema does not occur in firm, inextensible parts (compact substance of bone, cartilage, tendons).

Concerning the amount of water in the brain in typhoid fever, see BUHL, *Z. f. rat. Med.*, 1858, IV., p. 304.

MICROSCOPICAL EXAMINATION of œdematous parts wholly or chiefly consisting of connective tissue shows the connective tissue fibres separated from one another to a greater or less extent by a liquid sometimes very poor, sometimes very rich in lymph-corpuscles, clear, or giving with alcohol a molecular coagulation. The fixed connective tissue corpuscles are often large, oval or flattened. The appearances rarely lead to the inference of an undoubted filling of the lymphatic capillaries. For the most part only the adventitia of the vessels are much distended and separated from the vessels to which they belong, especially in the mucous membranes, and in the brain. Hence the connective-tissue fibres are frequently somewhat clouded. The histological relations of the remaining œdematous tissues, especially of those consisting of cells, are not yet sufficiently known. Epithelia resist for a long time the distention of their bases, until they for the most part undergo atrophy, rarely becoming œdematous. A similar simple atrophy is exhibited in the gland-cells of the liver and kidneys. In the fat-cells the fat becomes more and more scarce, until finally the cell-membrane contains only the nucleus and serum.

W. YOUNG (*Wien. Sitzgsber.*, 1868, May) examined the œdematous skin of the scrotum, finger, knee, the lymphatics of which he had injected with Prussian blue. By this the lymphatics in the corium were found to consist in many layers of a thick net-work, and in the upper layers of the corium limited by epithelial cells alone, in the lower layers by these and an elastic network. In the upper layers of the corium they are accompanied here and there by one, in the lower layers by two bloodvessels. Bloodvessels ensheathed within lymphatics have not been observed by the author. Œdematous fluid is found chiefly in spaces through which pass connective-tissue bundles, isolated connective-tissue cells and fibres, and which are limited not by a special membrane, but by one formed nearly of epithelium. In these spaces the free,

round, oval or somewhat spindle-shaped cells (migrating or exudation cells) are found most abundantly near the bloodvessels.

According to RANVIER (*Compt. rend.*, 10 July, 1871) the bundles of œdematous connective tissue are after 15–20 hours separated from one another by a clear serum; in this float numerous white blood-corpuscles with amœboid movements. The fixed connective-tissue cells, which in the normal state are flat, hyaline, large and stretched on the surface of the connective tissue bundles, are spherical and filled with strongly refractive granules. The fat-cells around their characteristic fat-drops show similar strongly refractive granules, resembling a string of pearls. The capillaries, like the small veins and arteries, are distended by blood, their inner surface covered with numerous white corpuscles. The granules of the fixed connective tissue cells, like those of the fat-cells, are round; they refract the light more strongly than albuminous, less than fatty granules. With acetic acid, etc., they become smaller, more strongly refractive, and resemble finely-divided fat.

DROPSY OF SEROUS CAVITIES is likewise a pathological collection of quantitatively and qualitatively changed liquid. In most of these cavities their communication with the lymphatic net-work, and the taking up of fluid and solid substances into the latter, has been experimentally demonstrated. (See p. 150.)

Consult particularly RECKLINGHAUSEN, DYBKOWSKY, LUDWIG, and SCHWEIGGER-SEIDEL (*Ber. d. S. Acad.*, 1866).

The serous membranes in dropsy, when no complication (inflammation, etc.) exists, are pale, anæmic, cloudy, thinned, or somewhat thickened, less elastic. Their endothelia are more easily separated, often increased in size, of less regular form, of a finely granular appearance. The lymphatics are not infrequently clearly dilated. The tissue of the serous membranes sometimes exhibits fatty metamorphosis of its cellular elements, otherwise nothing abnormal. The muscular tissue surrounding them is pale; after a longer duration, it becomes affected by simple atrophy, or by fatty degeneration.

The changes in the brain-substance about the ventricles in acute hydrocephalus are for the most part not effects of the dropsy, but concomitant effects of the inflammation. In chronic hydrocephalus, externally (œdema of the pia-mater) as well as internally, a diminution is observed in the size of the brain-mass to so great an extent that it becomes reduced to the thinness of paper. It is thereby not infrequently rendered firmer. Sometimes, however, softening of the surrounding brain-substance occurs, which perhaps is cadaverous in nature.

Very similar to dropsy, but to be distinguished from it, are: 1. FALSE dropsies or cysts, which result from closure of the excretory ducts of certain glandular organs, mucous membranes, or *diverticula* of normal mucous membranes, and which, after a longer time, contain only a serous or sero-mucous liquid with or without traces of the former normal contents; renal dropsy or hydronephrosis; dropsy of the gall-bladder, Fallopian tubes, uterus, vermiform process, lachrymal sac; the cysts arising from closure of the excretory ducts of mucous glands. 2. WATERY SECRETIONS ON FREE SURFACES, especially of mucous membranes, *e.g.*, of the intestinal canal in many catarrhs of that tube, in cholera, etc., as well as of many glands (*e.g.* of the salivary glands in salivation). In not a few cases, during life as well as after death, it is impossible to say whether the secretion, *e.g.* of a parenchyma or serous cavity, is a TRANSUDATION (dropsical liquid), or EXUDATION (see INFLAMMATION). NO SHARPLY-DEFINED LINE SEPARATES THESE TWO. The liquid of blister-vesicles, *e.g.*, is sometimes analogous only to blood-serum, *i.e.* relatively rich in salts, moderately albuminous, but very poor in fibrinogenous substance; some time, on the other hand, it is very rich in albumen and proportionately so in fibrin. The tendency of the liquid to coagulate increases if the SAME part be subjected to a quick succession of blisterings; for the repeated irritation is accompanied by more extended circulatory disturbances than a single irritation. (O. WEBER.)

The LIQUID in DROPSY, ŒDEMATOUS or DROPSICAL TRANSUDATION, is colorless or light yellow, clear and transparent, of insipid or slightly saltish taste, with an alkaline, very rarely with an acid reaction, and with a specific gravity slightly higher than that of blood-serum.

Its CHEMICAL CONSTITUENTS are :

WATER, about 95 % ; thus in greater quantity here than in blood-serum (which contains about 91% of water), less in older liquids.

ALBUMEN : next to water in importance in most dropsical liquids ; in very small quantity in the dropsical liquids of the brain and spinal cord. Its quantity stands generally in inverse proportion with its salts, in almost direct ratio with its contained fibrinogenous substance. In greater quantity it is the cause of the viscidity or frothiness of the liquid.

C. SCHMIDT in a case of Bright's disease found 2.85% of albumen in the liquid of the pleura, 1.13% of it in that of the peritoneum, 0.6–0.8% in that of the cerebral meninges, 0.36% in that of the subcutaneous cellular tissue. If also these quantities vary in different cases, the proportion of the albuminous contents of the transudates in different localities in the same individual always remains the same (HOPPE, l. c. IX., p. 241 et 258). Besides, HOPPE (Deutsche Klinik, 1853, p. 44 ; Virch. Arch., XVI., p. 391) found for the most part, the transudates in quickly repeated punctures less albuminous ; more rarely (Virch. Arch., IX., p. 240) was the albumen more abundant in the second puncture, if the quantity of the transudate and the pressure had increased. HOPPE found in œdema of the feet, free from blood-corpuscles, only 1.7% solid ingredients and only 0.3% of albumen.

The quantity of albumen is dependent : 1. Upon the capillary system, by means of which transudation takes place (C. SCHMIDT) ; 2. Upon the quickness of the blood-circulation, so that the transudate is rich in albumen in direct ratio with the slowness of the blood circulation in the capillaries (LEHMANN) : if the circulation in the abdominal veins be considerably retarded by large tumors, the pressure increases and albumen in larger quantities will be found in the transudate, than when mechanical hindrances of less importance, as e.g. affections of the liver with contraction of the parenchyma, etc., are the occasion of a slower venous circulation (less elevation of pressure) ; in acute hydrocephalus the quantity of albumen is greater than in the chronic form ; 3. Upon the character of the blood ; the poorer the blood is in albumen, as e.g. in Bright's disease, so much the less is found also in the transudate ; 4. Upon the duration of the dropsy, since in long duration, and from the time in which the pressure of the transudate and that of the blood become equalized, salts and water return into the blood, whilst the albumen, which can penetrate through membrane only under positive pressure, remains behind and becomes relatively increased. (HOPPE.)

The mucous consistence, which the liquid of ovarian dropsy often shows, is not dependent upon the presence of mucin, but upon that of peculiar albuminous bodies (metalbumen and paralbumen of SCHERER).

FIBRIN, as such, i.e. as a combination of fibrinoplastic with fibrinogenic substance, flocculent in form, or as a uniform gelatinous substance, seldom occurs in dropsical liquids. Sometimes it is secreted only after long standing. But all transudates contain, for the most part proportional to the albuminous contents, therefore in very small quantity, FIBRINOGENIC SUBSTANCE. Fibrinogen is most abundant in the liquid of the pericardium, and of hydrocele. It is not secreted in solid form, because the fibrinoplastic substance is not simultaneously present in the transudate. The latter may, by the addition of blood, almost instantly be coagulated.

SCHMIDT has examined in all 93 transudates with respect to their fibrinosity : 12 liquids from hydroceles, 42 from the pericardium, 15 from the pleura, 16 from the peritoneum, 1 from the cerebral cavities, 1 from the cellular tissue of a new-born child, 3 from blisters, 1 from a hygromatous cyst, 1 from a vesicle by cold, 1 as synovia from an inflamed knee-joint. In 81 of these cases coagulation occurred through contact with blood. In 11 cases coagulation could no longer be produced.

Here, however, exhaustive hæmorrhages within the body had previously occurred (in the living body, or in the dead body, so that the serum had escaped through the dead vascular walls), or in its escape during life or during the autopsy the blood had induced coagulation. The greater number of exceptional cases in no way concern liquids poor in fibrin or albumen : these, on the contrary, were concentrated, but came from organs which before death had suffered from inflammation. Very frequently, liquids coagulate spontaneously after their escape from the dead body, usually after their secretion from the body had taken place ; they do not appear before 1–1½ hours, often not until after 8–10 days.

In the fluids of the dead body coagulation never fails, at least to the extent of slight cloudiness, while from the living often perfectly clear fibrinous liquids are taken, which, until putrefaction begins, remain free from all spontaneous coagulation. It must therefore be assumed, that in the dead body coagulation takes place because of the slight transudation of fibrinoplastic substance through the dead vascular walls. Coagulation within the body is effected by the blood-serum, which trickles through the vascular walls, in lymphatic dropsies (VIRCHOW) through access of blood during operations or already accomplished in the body.

Punctures, quickly made in succession, of dropsical serous cavities are generally followed by an increase not only of the albuminous, but also of the fibrinous contents of the transudate (see p. 227).

According to NAUNYN (*Dorp. med. Ztschr.*, 1870, I., p. 174), the transudates in ovarian cysts, in amyloid degeneration, also those of the peritoneum, are frequently perfectly clear, or only slightly opalescent and not viscous, of very low specific gravity, coagulate either spontaneously or after contact with fibrinoplastic substance, and, when boiled after acidification, do or do not let fall albumen, and reduce alkaline solutions of copper.

HENLE (*Hdb. d. Anat.*, 1871, III. B., p. 312) characterizes the subarachnoidal connective-tissue bands and meshes as a physiologically dropsical connective tissue. The cerebro-spinal fluid approaches chemically most nearly the liquid of œdematous connective tissue : it contains, in contrast with the liquids of the serous cavities (pleura and peritoneum) few solid ingredients, namely little albumen and no fibrinogen.

EXTRACTIVE MATTERS, in varying, for the most part proportionately large quantity, proportionate to the age of the dropsical fluids, sometimes amounting to 4–8.6% of the albumen. There are present coloring matters of unknown nature, which are the cause of the different coloring of the liquid; sometimes the coloring matter of the blood and bile.

FATS, in small quantity in recent, in greater quantity in old dropsies; almost constant in small quantities, often in very large quantities in dropsy of the scrotum.

UREA, uniformly present, in large quantity in Bright's disease.

LACTIC ACID (in puerperal fever), and uric acid are not infrequently to be recognized.

Xanthin, creatin, and creatinin are occasionally present.

BILIARY SALTS, as well as the coloring matter of bile, in dropsy through diseases of the liver, and diseases with icterus.

SUGAR, constant in diabetes mellitus, otherwise rare.

SOLUBLE SALTS, especially chloride of sodium, besides carbonates, phosphates, sulphates, mostly of soda, in less quantity, of potassa, lime, and magnesia, are always found in almost the same proportion as in blood-serum, in quantity proportionate to the water of the blood, and to the richness of the transudate in albumen.

In Bright's disease, the quantity of salts in the transudate may outweigh that of the organic material. In hydrocephalus, phosphates and compounds of potassium prevail. (C. SCHMIDT.)

AMMONIA occurs in transudations, as in the liquids of the body, at the most in extremely small quantity.

GASES, carbonic acid, oxygen, and nitrogen, in small quantity.

NORMAL LYMPH consists of a colorless plasma and lymph-corpuscles, as well as for the most part of fine oil-globules. Plasma contains fibrinogen and fibrinoplastic substance (the latter in less quantity than the blood), as well as, with the exception of the coloring matter, the remaining constituents of the blood : water, salts, albuminates, protagon, fats, urea, extractive matters, sugar.

The following table shows the COMPOSITION OF SOME OF THE TRANSUDATES, in comparison with that of blood-plasma, etc. (O. WEBER, l. c., p. 215) :

	Water.	Solids.	Albumen.	Fibrin.	Salts.
Blood-plasma..............	901,51	98,49	81,92	8,06	8,51
Blood-serum	907,60	93,40	77,62	———	9,45
Pus......................	871,50	128,58	68,66	———	10,50
Secretion of wounds.......	939,20	60,80	45,00	traces	8,90
Liquid of blisters..........	932,98	70,35	61,85	"	8,39
" hydrocele........	940,08	59,92	49,88	———	———
Pleural transudate.........	945,15	54,85	26,74	0,60	8,17
Pericardial "	965,11	34,89	20,15	———	———
Peritoneal "	962,67	37,33	17,91	———	8,11
Anasarca "	930,97	19,03	18,37	———	8,22
Cerebro-spinal fluid........	986,36	13,64	3,16	———	8,35

The fluid from the hip-joint in a case of *arthritis deformans* contained 23,2 mucin, 20,9 albuminous material, 8,8 inorganic matter, 942,7 water (HOPPE-SEYLER, *Virch. Arch.*, 1872, LV., p. 253).

The MICROSCOPIC ELEMENTS of transudates are very few. The only elements which are ESSENTIAL and CONSTANT, but in variable quantity, are the LYMPH-CORPUSCLES. By the more recent knowledge of their circulation (see p. 152), and of the pathogenesis of dropsy given above, their constant occurrence, as well in œdema as in dropsy, is easily explained. ENDO-THELIAL CELLS of the affected serous membranes, sometimes CRYSTALS OF CHOLESTERIN, etc., are ACCIDENTALLY present.

Sometimes the dropsical fluid has a THIN MILKY character. especially in the abdominal cavity ; it proceeds either from a mixture of fat, or from a peculiar combination of albumen (A. SCHMIDT'S molecular fibrin). Sometimes the character of the transudate is that of a thin mucus.

CAUSES OF DROPSY.

The causes of dropsy in general are always CHANGED CONDITIONS of CERTAIN ORGANS, or of the BLOOD, or of BOTH AT THE SAME TIME. The affected organs, particularly, are the heart, next the veins and lymphatics, the kidneys, the lungs, and the liver. The blood-changes consist in a diminution of albumen, and in an increase of water. In many cases of dropsy the BLOOD-CHANGES are dependent upon a PREDISPOSITION, while a MECHANICAL CIRCUMSTANCE determines the OUTBREAK. The mechanical condition consists either in an increased abstraction of fluid from the blood, or in an absolute or relative diminution of the resorption of the excreted liquids not used in cell-formation. Increased separation of liquids depends : either upon an increase of local blood-pressure through arterial, especially, however, through venous hyperæmia ; or, upon a diminution of the tension of the tissues surrounding the capillaries (*e.g.*, by the cupping-glass, or Junod's boot) ; or, upon a relaxation and resulting greater porosity of the vascular walls. Diminished resorption is dependent upon an increased local blood-pressure, as well as upon the character of the liquid.

With respect to blood-changes, the dropsical or serous crasis, which is a consequence of dropsy, must be distinguished from the primary blood-changes which are the cause of dropsy.

Transudation is a FILTRATION of blood-serum through the capillaries, occurring under increase of the pressure in the vascular system. All the truly dissolved matters of the blood, as salts, fat, urea, pass through in the same proportions as they occur in the blood. The matters not in true solution contained in the blood, the albumen and the fibrinogenous substance, as well as the corpuscular elements, pass through in much less quantity. Besides filtration, the laws of DIFFUSION, of the interchange of fluids through membrane, enter into consideration. Out of the blood salts as albuminates are much sooner diffused into the fluids of the tissues. If the surrounding liquid be slightly acid, under similar conditions and in the same time less albumen will pass through the membranes, than if that liquid be neutral or alkaline (HEYNSIUS).

1. MECHANICAL DROPSIES.

They arise mostly through hindrance to the return current of venous blood or of lymph, less often through active hyperæmia. Their starting-point is the blood- and lymph-capillaries. The escape of water is IN CONSEQUENCE OF THE ELEVATED PRESSURE, which the increased vascular contents exercise upon the vascular walls.

Through VENOUS, or MECHANICAL HYPERÆMIA (see p. 183) arise either local œdemata, or dropsies of single serous cavities, or general dropsies. According to the older view simple disturbances of circulation were sufficient to produce these effects; according to more recent investigations there must be present, at the same time, a paralysis of the vaso-motor nerves.

From an experiment by LUDWIG and TOMSA, it resulted that after moderate contraction of the veins of the *plexus pampiniformis* more lymph flowed out than while the venous stream was unimpeded : the increase amounted in the mean, in three animals, to 59 p. ct. of the quantity of lymph which, before or after the ligation, flowed from the perfectly free plexus. Were the veins coursing in the plexus entirely closed, so that the blood-stream, returning from out of the testicle, was conducted into small efferent branches, then the increase in five animals amounted in the mean to 3.7 times that which escaped in the uncontracted blood-stream. NASSE (l. c.) found, during periodical compression of the external jugular vein, the lymph-stream increased 10-30 per cent.

RANVIER (*Compt. rend.*, 1869, LXIX., No. 25) has again experimentally demonstrated the correctness of the theory founded on LOWER's experiment, concerning the origin of œdema : ligation of the inferior vena cava within the thorax is a too great operative procedure ; that of the jugular veins gave R. negative results. R. found in dogs, whose inferior vena cava he had ligated, that œdema of the lower extremities appeared only when the ischiatic n. was at the same time cut. If this nerve was cut on one side, œdema appeared only on that side, and already within 1-2 hours, while the other side remained free : one hour after the section swelling manifested itself about the *tendo achillis ;* one hour later the subcutaneous connective tissue was slightly infiltrated ; 20 hours afterward the whole limb was cylindrical and strongly infiltrated with serum. In a dog, which was not killed, the œdema lasted three days, on the fourth it decreased, on the fifth it had disappeared. Section of the last lumbar, and of the sacral nerves within the spinal canal, or of the spinal cord above the lumbar swelling, was not followed by these results. Hence R. concluded that a PARALYSIS OF THE VASO-MOTOR NERVES (those from the sympathetic follow the course of the sciatic) MUST BE ADDED TO THE VENOUS STASIS IN ORDER TO CAUSE DROPSY.

GOLTZ (*Arch. f. d. ges. Phys.*, 1871, V., p. 53) found that in a frog deprived of its brain and spinal cord he did not succeed by transfusion in restoring the circulation, because the liquid flowed out of the dilated vascular wall as if through a sieve ; the veins were widely dilated and all organs were covered with a free liquid of a blood color. Whether this increased transudation is to be explained by the thinner walls or by the loss of the direct influence of the nerves, is questionable.

Local œdema from venous hyperæmia, mostly with dilatation of the veins, is very

frequent, and affects particularly the region of the inferior cava. It arises after contraction of the veins from external pressure (see p. 184; in this we have also the explanation of the frequent tumors on the head of the new-born), or during the formation of cicatrices, from tissue-changes in the venous walls (cancer), from venous coagula, etc. The conditions mentioned give rise to œdema, either without the assistance of farther causes, or only after their appearance: manner of life, unsuitable clothing, convalescence, hydræmia, chiefly. Many, especially large and vascular tumors, act not only mechanically through pressure, but also by extending the course of the blood by the interpolation of a second system of capillaries.

DROPSIES of SEROUS CAVITIES arise less often through passive hyperæmia: hydrocele through phlebectasis of the affected vessels, ascites through contraction of the trunk, or of many branches of the portal vein; internal hydrocephalus through tumors at the base of the brain, which compress the *vena magna Galeni*, or the straight sinuses, etc. Dropsy of the hernial sac also has this origin.

In many of these cases the appearance of dropsy is prevented or delayed by the formation of collateral currents. In the greatly obstructed passage of the blood of the portal vein through the liver. *e.g.*, in cirrhosis of the liver, there appears first of all a dilatation of the portal vein and of its abdominal roots; afterward a dilatation of numerous small vessels, by means of which the portal is connected with the caval system, so that the blood of the portal vein, evading the liver, reaches the vena cava.

GENERAL DROPSY, from venous hyperæmia, is found in many diseases of the heart, because of the obstruction to the return of venous blood into the right side of the heart. Especially do chronic peri-, myo- and endocarditis here enter into consideration, giving rise to insufficiency and stenosis. Dropsy has a direct origin in insufficiency of the tricuspid valve. which prevents the return of the blood from the right side of the heart, and consequently the EXIT of the blood into the great veins of the body; an indirect origin in insufficiency of the mitral valve, which gives rise to engorgements in the lesser circulation, and through the pulmonary artery, also in the right side of the heart and in the veins. Still more indirect is the effect of affections of the aortic valves: dropsy appears quite late and probably only through the diminished *vis a tergo*.

ARTERIAL HYPERÆMIA gives rise to the diagnostically important COLLATERAL ŒDEMA, which is a result of increased lateral pressure in the capillary vessels (see p. 180). The same occurs most often in the neighborhood of inflamed parts: *e.g.*, œdema in the vicinity of erysipelas and pseudo-erysipelas; œdema of the surface of the trunk and of the extremities, during the presence of deep abscesses; œdema of the prepuce in chancres of the part; œdema of the face and mouth during suppuration; *œdema glottidis* in catarrh and ulcers of the neighboring parts of the larynx; subcutaneous œdema of half of the thorax during pleural empyema.

The influence of arterial hyperæmia upon the flow of lymph is not so constant as that of hyperæmia of engorgement. It depends upon the fact that through the dilated arteries a larger and quicker blood-current flows into the capillaries. When LUDWIG, after section of the cervical sympathetic, compared the quantity of lymph obtained with that previously separated, the separation in some cases was found not inconsiderably hastened, in others this result was not obtained. Redness of the skin and increased lymph-formation often appear together. Swelling of the leg of a frog will follow the dipping of its foot into a strong solution of common salt (NOTHNAGEL).

According to RINDFLEISCH (*Lehrb. d. path. Gewebel.*, 1873, p. 583), effusions in internal hydrocephalus do not proceed from changes of the ependyma, but from strong hyperæmia of the normal or enlarged papillæ of the choroid plexus.

When the RETURN FLOW OF LYMPH is PREVENTED, as *e.g.*, by thrombosis of the lymphatics, by suppurative or carcinomatous infiltration of their wall, or of the lymph-glands, dropsies rarely occur: in part because of the extensive anastomosis of the lymphatics at their origin, in part because a rise in the pressure under which the parenchymatous liquids exist, is fol-

lowed by increased resorption through the lymphatics, in part because the veins, during an obstruction of the lymph-flow, perform the function of the lymphatics.

According to MEDER (*Ztschr. f. rat. Med.*, 1860, X., p. 323), the lymphatics perform no act of resorption after ligation of the aorta; but, wherever resorption follows, it is rendered possible by the bloodvessels, which are given off above the point of ligature and extend so far downward that they come in contact with the liquid mechanically diffused upward.

VOLKMANN (*Berl. klin. Wschr.*, 1870, No. 30 u. 32) observed in sick persons, who on account of traumatic or inflammatory affections were compelled for weeks or months to hold a lower extremity immovably in an extended position, frequent acute or chronic hydrarthus immediately after the first attempt at motion.

A LOCAL dropsy is quite rarely dependent upon the lymphatics alone. In a number of cases attributed to this relation, there is found a simultaneous obstruction of the venous circulation, or a change in the lymph-glands, as is *a priori* probable from the near relation of the veins and great lymphatics on the flexor side of the extremities (inguinal region, axillary space, etc.). Other cases are, without safe anatomical grounds, referred to contraction or inflammation of the lymphatics: thus elephantiasis, *phlegmasia alba dolens*, epidemic parotitis, induration of the connective tissue in the new-born. On the contrary, the lymphatics, especially the retro-peritoneal and inguinal, are in most cases of œdema found remarkably dilated and filled to distention with clear liquid: this does not, however, so much demonstrate their increased activity, as the opposite (consequences of diminished elasticity and tonicity of their own walls, of diminished muscular movement in the extremities, respiratory organs, heart).

ENGORGEMENT OF THE OPTIC PAPILLA, ophthalmologically and circumstantially, also clinically, important, has its origin most frequently in an increased collection of fluid in the subvaginal spaces, *i.e.*, in the spaces opening directly into the arachnoidal space of the brain between the outer and inner optic sheaths. (Experimental and clinical investigations of GRAEFE, MANZ and others.)

Only in very rare cases of general dropsy was it dependent upon a closure of the thoracic duct. WRISBERG, SCHERB, FR. NASSE observed it in man, VIRCHOW in a new-born calf. Rather, dropsy in narrowing or closure of the thoracic duct not infrequently is entirely absent (VIRCHOW, OPPOLZER, and others), because still other inosculations of the lymphatics with the blood-stream are present.

DISEASES OF THE SEROUS MEMBRANES, especially thickening of them after inflammation, tuberculosis, cancer, give rise with comparative rareness to dropsy of those membranes, yet oftenest in the *tunica vaginalis* and in the knee-joint. Dropsies of this kind pass by undetermined limits into inflammations with serous exudation.

The explanation of these dropsies becomes easy from our present knowledge concerning the structure of serous membranes. And yet detailed investigations are still wanting. These dropsies occur either in such a manner that beside the diseased serous membranes the remainder are normal (hydrocele, *hydrocephalus internus chronicus*, peritoneal tuberculosis, peritoneal cancer), or so that the other serous cavities contain much less water (most frequent in higher grades of hydropericardium).

In dropsies arising from DISEASE OF THE GLANDS, as well of the liver, spleen, and kidneys, as of many lymph-glands, there is added to the pure mechanical condition of vascular contraction after a longer time the dyscrasic—hydræmia. The mechanical force consists in contraction of the capillary vessels, small arteries and veins. This is dependent above all upon degeneration of the bloodvessels, especially the lardaceous, as well as upon hypertrophy and cicatricial contraction of the connective-tissue portion of these glands with simultaneous atrophy of the vessels and glandular elements (granular liver, granular kidneys).

DROPSIES AND ŒDEMA EX VACUO occur as œdema of the pia mater of the

brain, and dropsy of the cerebral ventricles in general and partial atrophy
of the brain, as quick re-collection of fluid in a serous cavity, which was
dropsical, after evacuation of that fluid, as hydropericardium in a diminu-
tion of the size of one or of both lungs.

2. CACHECTIC DROPSIES.

These arise in CONSEQUENCE OF A CACHEXIA, hydræmia, *i.e.*, of a decrease
of the albuminous, and increase of the watery contents of the blood. In
reality, they occur but rarely by themselves, whilst in most cases either
simultaneously and from like cause a mechanical force is present, or whilst
the latter arises in consequence of the cachexia and is the special cause of
the serous secretion. (See Hydræmia.)

The purest cachectic dropsies are those, which, continuing for a long
time, originate in conditions connected with INSUFFICIENT NOURISHMENT
and digestion, or with large hæmorrhages, or other losses in other ways of
albuminous matters.

Dropsy in consequence of INSUFFICIENT NOURISHMENT (inanition) is very rare.
Perhaps to this cause are due those cases, which in years of famine appear epi-
demically, *e.g.*, in 1771 in Eichsfeld (ARAN). VIRCHOW observed this dropsy neither
in the epidemic of Upper Silesia, nor during the famine in Spessart. In the
bodies of individuals who have died of cancer of the œsophagus or stomach with
considerable stenosis, for the most part no œdema has been found, at the most very
little of the ankles, marked only in complications.

In CONVALESCENCE, especially after acute diseases of long duration,
œdema of the lower extremities appears very often, if at the same time the
nutritive supply is insufficient, or, if during a full supply mechanical forces,
as sitting and standing, assist (*hydrops gravitativus*).

HÆMORRHAGES of all tissues, if they are at once profuse, and still more
if they often recur in greater or less quantity, are not rarely causes of
dropsy.

LONG CONTINUING SUPPURATION of the skin and of the bones, mucous
discharges from the nose, intestine, genitals, suppurations of simple,
dysenteric, chronically syphilitic, tuberculous and cancerous nature, espe-
cially of the mucous membranes, more rarely in serous membranes (sup-
purative exudations of the pleura, etc.), and in parenchymata, are likewise
not infrequent causes of dropsy,—frequent, however, with simultaneous fatty
degeneration of the vessels of the large glands.

ALBUMINURIA is one of the most frequent causes of dropsy. Its general
causes are not yet known: it can have its origin either in such changes of
the membranes between the blood and the urine, that they permit the
albumen of the blood to pass over into the urine (increased tension in the
arterial, or engorgement in the venous system); or it has its origin in
changes in the property of diffusion of the albumen of the blood. Dropsy
in albuminuria is a consequence of the thinning of the blood-serum, which
again is dependent partly upon the loss of albumen, partly upon the accu-
mulation of water in the blood.

The kidneys have a double function: they separate the specific elements of the
urine from the blood, and they are the regulators of the watery contents of the
blood. Through disturbance of the first arises uræmia, through that of the second
dropsy. The latter is met with most regularly and largely in the second stage of
Bright's disease, less often, and for the most part in less degree, in granular kidney.
In the former the quantity of albumen may reach to three per cent. and more, which
daily amounts to twenty grammes and over; in the latter it is very much less. The

causes of albuminuria in granular kidney lie in the very high blood-pressure: animal membranes, which under a moderate pressure of liquid are impermeable to albumen, etc., let small quantities of it pass through under increase of the pressure of filtration. In the second stage of Bright's disease albuminuria is probably dependent upon the inflammatory changes of the uriniferous tubules. (BARTELS, in VOLKMANN's *Klin. Vortr.*, 1871, No. 25.)

To the cachectic dropsies belong also those of SCORBUTUS and conditions resembling it, which latter are secondary to many chronic and some acute diseases; besides those in MALARIAL CACHEXIA; as well as finally those after chronic POISONING with arsenic, etc.

DROPSIES FROM UNKNOWN CAUSES are found after taking cold, after the quick disappearance of cutaneous eruptions (acute and chronic), after quick healing of cutaneous ulcers, in suppression of menstruation. Many of these dropsies are of congestive origin.

In a number of these cases there exist perhaps the causes of dropsy above-mentioned, and the latter even from the same causes, *e.g.*, quick healing of cutaneous ulcers, suppression of menstruation, and hæmorrhoids (primary dropsy). At other times the dropsy is dependent upon the kidneys, whilst the causes of disease, *e.g.*, the *contagium* of scarlet-fever, acts not only upon the skin and throat, but also upon the kidneys.

Not more certainly known is the pathogenesis of the not infrequently acute dropsies, appearing especially in tropical countries (so-called ATMOSPHERIC DROPSY). Probably these also are for the most part of congestive origin, and are consequences of direct or reflex nervous influence, perhaps sometimes also immediate consequences of arrested cutaneous function.

According to DE HAEN almost the whole army of Charles V., in the expedition against Tunis, became dropsical through cold drink after long abstinence. During the more recent campaigns of the French in Algiers, œdema not infrequently appeared suddenly, mostly in the face, neck, fore-arms, hands, legs and feet, which in subsequent continuous warmer weather by degrees disappeared of itself. Also in the natives of Africa sometimes sudden and very large œdema of the scrotum arises, if they are overtaken by the rain during work.

At other times blood-changes are simultaneously present: in chlorosis acute œdema of those parts which are exposed to the air; œdema in scorbutus; œdema in snakebite; œdema in the pregnant also without albuminuria.

In our own region also, there is observed, in renal diseases already present, an influence of the air upon the origin of dropsical swelling: *e.g.*, œdema of the face in Bright's disease, which is exposed to the air at the usual or colder temperature; likewise œdema of the face, of the eye-lids, of the neck and of the upper part of the breast in the chlorotic from like causes, with for the most part quick disappearance (ŒDEMA FUGAX).

The causes of the following dropsies are likewise unknown: *hydrops spasticus* or *hystericus ; hydrops paralyticus* (œdema in the paralyzed half of the body); *hydrops irritativus*, as a consequence of slight irritations of the skin, which at other times produce only partial redness and infiltration, in individuals with irritable skin.

Dropsy of the face was seen by myself in a case of a child four years old after two half-grain powders of morphine: it disappeared after about twelve hours. For days thereafter it again appeared after the half dose and had an equal duration.

The causes of the œdema of the face and extremities occurring almost constantly in extensive INFECTION WITH TRICHINÆ, lie, according to COLBERG, in the destruction of the capillaries of the muscles in the part affected by the wandering trichinæ and the tissue surrounding them; the œdema disappears with the establishment of the new capillary net-work. According to KLOB (*Oestr. Jahrb.*, 1866, 4. u. 5. H., p. 98), œdema in trichinosis is not a consequence of collateral hyperæmia, but dependent either upon lymph-thrombosis of the finer vessels, or upon the fact that the trichinæ make use of the lymph channels for their wandering. Besides also upon the fact that the muscular co-operation in the motion of the lymph is destroyed by the

trichinous affection of the muscles directly at one time, when in consequence of the irritation of the tissues transudation is increased.

SYMPTOMS OF DROPSY.

SYMPTOMS OF DROPSICAL INFILTRATION.   The œdematous parts are en-larged, paler, more or less translucent, mostly doughy to the touch, rarely harder.   The skin, or mucous membrane, or serous membrane covering them is smooth, without wrinkles, non-vascular, thinned.   The proper warmth of the parts is, in consequence of the retarded circulation of the skin, diminished.   The parts pit under pressure by the finger, as well as from pressure of other kinds, *e.g.*, by the clothing, folds of bed-clothes, etc., the usual level of the surface being slowly regained.

In general œdema the various parts of the body are œdematous always in different degrees.   The œdema affects least, in the usual position on the back, the head and the upper and anterior halves of the trunk; more decidedly, the upper extremities; it is most developed in the lower portion of the abdomen, in the genitals, and lower extremities.   In local (with the exception of the arterial form) as well as in general œdema, the œdematous liquid sinks to the lowest parts of the body: in sitting, into the legs; in lying, according to the position on the back or side.

All these symptoms are intensified in proportion to the length of time they exist; there appear also disturbances in the nutrition of the parts, as decrease of adipose tissue, diminution of the gland-cells, laceration of the vessels and even of the skin (false cicatrices of the abdomen and upper part of the thigh).

In œdema, still other disturbances have their origin, which are in part general, in part and especially local.   The latter are: feelings of tension, of weight, which are intense in proportion to the acuteness of the œdema, deficient suppleness of the surrounding tissues, and to the strength and sen-sitiveness of the individual; feeling of weakness in the muscles, especially of the extremities, diminished contraction of striped and smooth muscles; lessened excretion of the glands of the skin and mucous membranes, in consequence of pressure, anæmia, etc., (dryness of the skin and mucous membranes); narrowing of the openings on the surface, and of the canals: of the mouth, of the opening of the eyelids, of the termination of the urethra and vagina, of the throat, entrance to the larynx, glottis.   Besides, there arise disturbances of nutrition in consequence of compression, imbi-bition, maceration (in the neighborhood of the cerebral ventricles?). Sometimes it leads to watery effusion through the pores of the skin, also to laceration of the tissues, especially of the skin of the lower extremities, sometimes after previous formation of blisters with consequent trickling out of water; rarely with resulting gangrene.

The symptoms of œdema of the parenchymata (brain, glands), as well as those of pulmonary œdema, consist mostly in a very slight increase of their size, because this is usually prevented by the surrounding structures (cranium, capsule of the liver, etc.), chiefly in diminished or altogether suppressed functions.

The SYMPTOMS OF FREE DROPSY are: increase in the capacity of the cavities in proportion to the yielding of their walls (*tunica vaginalis*, abdomen, joints); a dull or empty percussion sound, at first in the depend-ent parts, with changes in the tone corresponding with the position of the person affected; fluctuation in cavities whose walls are supple and little distended; succussion of cavities containing at the same time free or con-fined air; diminished, or absent auscultatory symptoms (lungs, heart);

sometimes the position of the patient exerts a great influence over the greater distinctness of these symptoms; changes in position of the organs in the cavities inclosing or bordering upon them (lungs, intestines, heart, in dropsy of their proper cavities); dislocations of the diaphragm, liver, and spleen, of the pelvic contents, of the abdominal and thoracic walls, of the mediastina, pericardium, and heart, of the cranial arch. Finally, compression of these organs, and the resulting diminished or entirely destroyed capacity of expansion: lungs, heart, great abdominal glands, brain, testicles; or diminished contractility: heart, abdominal, and intercostal muscles; thence anæmia and even atrophy.

Besides, the symptoms of free dropsy include those from functional disturbances of the affected organs, caused by their diminished mobility; by changes of place, compression with consecutive anæmia and atrophy. The functions of the organs are in general rendered difficult: dyspnœa, digestive troubles, stupefaction, and paralysis, etc., are produced.

If dropsy appears in fœtal life, there arise still greater troubles, e.g., in internal hydrocephalus; if it sets in during the first period of fœtal life, hemicephalia and anencephalia.

In GENERAL DROPSY there is another series of symptoms, which are dependent upon the causes of dropsy or upon its consequences. The excretions are diminished: the skin is dry, inflexible, sometimes scaly; the mucous membranes are mostly dry, their secretion tenacious; the urine is scarce, dark, muddy, the stools constipated and hard. Not infrequently some secretions are, during the whole duration of dropsy, or from time to time, very abundant: diarrhœas, e.g., are met with, even where there is no affection of the intestines present; or more abundant clearer urine (in *diabetes albuminosus*); or abundant sputa (bronchitis).

Extravasations, and mixtures of these with accumulations of water, are sometimes found, particularly in primary, rarely in secondary blood-changes having their origin in dropsy, in œdema as well as in free dropsy.

The blood-changes in dropsy are very different, according as they are primary or secondary. Sometimes there appears in transudates, which are especially rich in water and salts, an inspissation of the blood with a preponderance of solid constituents.

COURSE AND TERMINATIONS OF DROPSY.

When the causes of dropsy persist, the farther transudation of serum goes on, until the tension of the œdematous or dropsical parts has become as great as the mean tension of the arterial system.

The dropsical fluid remains the same, where its quantity neither diminishes nor increases, in continually changing relation to the blood-vessels and lymphatics, *i.e.*, elements are always being taken up into the circulation, and these are again abstracted in less, equal, or greater quantity. In this case, not only the circulation is never entirely arrested in the parts about the water, but there is also an absence of the graver disturbances of nutrition in the œdematous tissues. In many cases there occurs a hypertrophy of the skin, connective tissue, etc., especially in the lower extremities (*elephantiasis Arabum*).

According to VIRCHOW, the long persistence of the liquid in dropsy of cavities is not difficult to conceive, especially if the walls of the cavities are very dense and thick, since it, by its pressure upon the walls, must render resorption difficult, and since

here often very advanced products of decomposition, *e.g.*, cholestearine, are found in
great quantities.

Dropsy is either ACUTE, *i.e.*, it lasts only a few hours, days, or weeks,
within which it disappears, or ends with death ; or it is CHRONIC, with a
duration of months and years, and, if general, usually has a fatal termina-
tion.

In some cases dropsy is INTERMITTENT, particularly those forms of it dependent
upon congestive hyperæmia, as well as those which are vicarious : we have seen such a
dropsy in the knee-joint, which had lasted a year, and which returned every 10 days,
and after 2 or 3 days again disappeared.   Similar cases have been communicated by
LOEWENTHAL and BRUNS.
The division of dropsies into acute and chronic is practically important.   Many
dropsies of slight grade have the shortest duration, like the puffiness of the face
during severe attacks of coughing, *e.g.*, in whooping-cough.   The division into active
and passive, into sthenic and asthenic dropsies, is of little practical importance and
wanting in principle.   The earlier distinction between *hydrops calidus s. inflamma-*
torius, and *h. frigidus s. serosus s. torpidus* (to which most dropsies belong) now
again receives consideration.

Dropsies end in recovery or in death.

The TERMINATION IN RECOVERY, removal of the watery liquid, takes
place : rarely at once through PERFORATION OF THE WALLS OF THE CAVITY
exteriorly (in ascites, *e.g.*, through the navel, in spina bifida), or into the
surrounding connective tissue with consecutive resorption, or through per-
foration of the œdematous skin, and evacuation of the liquid ; sometimes
through BURSTING of the skin at many points, and gradual trickling off of
the liquid ; most frequently, comparatively, through quicker or slower re-
sorption.

The recovery is either genuine and permanent ; or, the dropsy after
shorter or longer time returns ; or, with especially quick resorption of the
liquid, œdema of internal organs (brain, lungs) appears ; or, from unknown
causes, death ensues.   Spontaneous quick decrease of the dropsy is con-
sidered an unfavorable omen, because the water may accumulate in more
important parts.   Usually, however, anasarca appears less sometimes be-
fore death on account of the collapse of the agony, because in the flaccidness
of the tissues it sinks into the deeper parts.

While general chronic dropsies have an unfavorable prognosis, there are many local
ones, *e.g.*, of the lower extremities, either without influence on the health, even for
many years, or which permit of palliative, rarely of radical help.

The TERMINATION OF DROPSY IN DEATH follows almost uniformly in all
general chronic dropsies.   It is because the DROPSY affects one or more
of the ORGANS ESSENTIAL TO LIFE (sudden death in œdema of the brain ;
quick death in pulmonary œdema, in œdema of the glottis ; slower death,
in the same conditions, in hydrothorax, hydropericardium).   Or, it is
dependent upon a CACHEXIA, which either has the same cause as the
dropsy (renal and hepatic diseases, etc.), or is a consequence of the dropsy :
hydrothorax, ascites, obstructed resorption of the lacteals and roots of the
portal vein, etc. ; erysipelas, suppurative inflammation, and gangrene of
dropsical parts ; inflammations of internal organs, etc.   Or it appears after
OPERATIONS, particularly punctures and quick evacuation of the cavities,
either without demonstrable cause, or in consequence of extensive hæmor-
rhage into the cavities, etc.

APPENDIX.

ACCUMULATION OF AIR, OR PNEUMATOSIS.

Consult DEMARQUAY, *Versuch einer med. Pneumat.*, transl. from the French by Reyher, 1867. Also the works on pathological anatomy, and on general pathology.

Pathological ACCUMULATIONS OF AIR occur in cavities and channels which contain air normally, as well as in those in which, under normal conditions, air is not found. Tissues and organs very rarely contain air, which in the normal state are free from it.

Accumulations of air in different parts of the body have for the most part special names : that of the pleura is called pneumothorax, that in the pericardium, pneumo-pericardium, etc. ; that in the cavity of the stomach and intestines, meteorism or tympanites, in that of the uterus, physometra ; that in the vesicles of the lungs, pulmonary emphysema ; that in connective tissue, emphysema or traumatic emphysema ; that in the interstitial or subpleural pulmonary tissue, interstitial or subpleural emphysema ; that in the blood, pneumathæmia.

I. Abnormal accumulations of air in localities which NORMALLY CONTAIN AIR admit of no general consideration. To these belong : increase of gases within the stomach and intestinal canal, especially of the large intestines (meteorism or tympanites), increase of the quantity of air in the pulmonary vesicles, with enlargement of them and atrophy of their partition-walls (vesicular pulmonary emphysema).

II. Accumulations of air in localities (cavities and parenchymata), which IN THE NORMAL STATE ARE WITHOUT AIR, have their ORIGIN in various ways.

a. The air is FROM WITHOUT, or FROM PARTS OF THE ORGANISM WHICH CONTAIN AIR, and PENETRATES into the parts affected. It enters either into cavities or into parenchymata.

The entrance of AIR INTO CAVITIES occurs : from without into the pleura, peritoneum, pericardium, into the vagina, into the uterus in a puerperal state, into cysts through accidental or operative wounds ; entrance of air into the veins, thence into the right cavities of the heart and into the pulmonary capillaries by wounds and operations, especially in the neck and upper extremities ; the entrance of air from the air-passages or lungs into the pleural cavities in wounds of both ; in perforation of emphysematous, tuberculous, gangrenous parts of these organs ; the entrance of air from the stomach and intestinal canal, rarely from the lungs, uterus, etc., into the peritoneal cavity.

In gynæcology, *garrulitas vulvæ*, so-called, the penetration of air into the vagina and its noisy escape, plays a rôle.

Of those cases in which EMPHYSEMA affects the PARENCHYMA, emphysema of the subcutaneous cellular tissue is worthy of notice. This arises : traumatically through the intentional blowing in of air, through penetrating wounds of the breast, fracture of the ribs, wounds of the laryngo-tracheal tube, through compound fractures of the extremities, through fractures in the nasal, frontal, maxillary and mastoidal regions ; not traumatically : in consequence of violent movements, long-continued screaming (in hydrophobia, during confinement) ; from escape of gas out of the digestive canal

after its adherence to the abdominal walls; through passage of gas from out of the larynx, trachea and bronchial tubes after perforation of them from various causes; through passage of gas from out of the lungs (tuberculosis, emphysema, gangrene, etc.).

Here also belongs emphysema of the mediastinum and skin, which occurs chiefly in children from whooping-cough and laryngeal croup, or, as also in the adult, from capillary bronchitis, etc. If many small bronchi are contracted or obstructed, the remaining parts of the lungs become so much the more distended, and single alveoli are lacerated ; the air then passes first into the interlobular or subpleural connective tissue, thence along the bronchi into the mediastinum, and finally into the connective tissue under the skin of the neck, always at first in the jugular region. Consult LAENNEC, ROGER (*Arch. gén.*, 1862, Aug. to Oct.), BARTELS (*D. Arch. f. klin. Med.*, II., p. 367).

The interlobular emphysema of very dry lungs, *e.g.*, in cholera, is, according to BUHL (*Lungenentz*, etc., 1872, p. 5), the atmospheric air in great quantity penetrating in visible vesicles into the lymphatics.

The mother-of-pearl appearance of the scales of psoriasis proceeds from the air which enters into them during drying (RINDFLEISCH).

Cases of emphysema of the liver are related by STOKES, LOUIS, PIORRY, HENOCH, FRERICHS, MEIGS (*Med. Ctrlbl.*, 1873, No. 3).

SCHATZ saw a case of fatal embolism by air which passed through the umbilical veins into the heart (*Mon. Schr. f. Geburtsk*, 1859, XXXIV., p. 112).

b. In localities air has its origin IN DECOMPOSITION OF MATTER THERE PRESENT : in the connective tissue of different parts of the body, especially the parts surrounding the urethra, through fetid decomposition or gangrene of abscesses, namely of those arising from interruption of continuity; in the abdominal walls; in various parts of the body during the existence of carbuncles ; in thrombi of the veins, which in rare cases are altogether emphysematous ; in the interior of serous cavities from decomposition of exudates there present ; in the cavities of mucous membranes normally empty of air (urinary bladder, uterus) from the same causes, or from putrefying blood-clots and fœtal remains, in the cavities of many cystic tumors.

Many cases considered in I. likewise belong here : Thus meteorism from long continuance of the fæces in the intestine. KLEBS (*Hdb. d. path. Anat.*, 1869, p. 284) distinguished two kinds of meteorism : the fermentation from increased formation of intestinal gases, and the mechanical from obstructed evacuation of the same. The latter is dependent either upon stenosis of the intestinal tube, or upon paralysis of the muscles of the intestines (stenotic and paralytic met.). Decomposition of food occasions the formation, within the stomach and intestinal canal, of CO_2 and H. Thus, *e.g.*, 1 atom of sugar=$C_6H_{12}O_6$ is decomposed into

$$2 \text{ at. lactic acid}=2(C_3H_6O_3) \quad = \quad C_6H_{12}O_6 \begin{cases} 1 \text{ butyric acid } C_4H_8O_2 \\ 2 \text{ } CO_2 \qquad\qquad C_2 \quad O_4 \\ 4 \text{ H} \qquad\qquad\qquad H_4 \end{cases}$$
$$\overline{C_6H_{12}O_6}$$
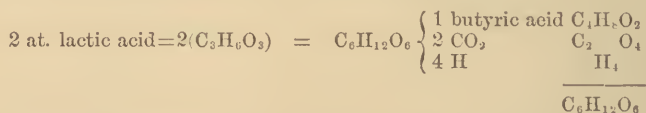
Besides, probably many cases of development of air in the blood may thus be explained, in which the air is formed almost always only after death (cases by DURAND-FARDEL, CLESS, etc.). In many cases attributed to this, the air has probably entered from without, or from air-containing parts of the organism. Consult the recent case by STOFFELLA (*Ztschr. d. G. d. Wien. Aerzte*, 1862, No. 22, 23 et 25).

c. The air is formed IN AN UNKNOWN MANNER. Here are referred those rare accumulations of air in the cavities of many mucous and serous membranes, those in the bloodvessels in many new-formations, for which none of the above-mentioned causes have been discovered.

The form and manner of the development of air in the last-mentioned series is still unknown : probably it depends upon a separation, a kind of secretion of the air by the bloodvessels. An analogue to this is furnished perhaps in the physiological occurrence of air in the cortex and marrow of hair, which in rare cases (KARSCH, BEIGEL, SPIESS) is so considerable that the hairs burst and break off above the level of the skin. Grayness of hair occurs usually through a change in the pigment-formation, less frequently without this through filling of the hair with air. Perhaps many cases of meteorism among the hysterical, of very quick appearance and without previous swallowing of air, may be explained in this manner.

Concerning the NATURE OF THE AIR little need be said in a general way. Atmospheric air entering from without sometimes undergoes changes similar to those of inspired air. The air arising from decomposition is like that in emphysematous gangrene. The constitution of air formed in an unknown manner is not yet known.

DEMARQUAY and LECONTE had already demonstrated, in 1859, that air injected into the cellular tissue or into the peritoneum was quickly changed in its constitution, lost a great part of its oxygen, and took up carbonic acid, the latter not sufficiently to replace the absorbed oxygen, but in return for which the nitrogen was considerably increased. This continues until the gas was absorbed. On the other hand, the authors have lately shown (*Compt. rend.*, 1862, LIV., p. 180) in a man whose cellular tissue became emphysematous from a fracture of the ribs, in 100 vols. of gas :

On the 4th day from injury, 2.54 CO_2. 6.35 O., and 91.11 N.
"   5th   "   "   5.08 "   4.66 "   "   90.26 "
"   7th   "   "   6.07 "   3.73 "   "   90.20 "
"   10th   "   "   11.11 "   0.00 "   "   88.89 "

THE GENERAL CONSEQUENCES OF ACCUMULATIONS OF AIR are those of a foreign body, which in part forces the tissues and cavities of organs asunder, in part causes inflammation of them, in part, finally (in the vessels) is quickly followed by death.

According to OLSHAUSEN (*Mon.-Schr. f. Geburtsk.*, XXIV., p. 350) the entrance of air into the puerperal uterus is hurtful, even fatal.

Quick exhaustion of the air by means of the air-pump is followed by development of the gases from the blood, embolism of the pulmonary and cardiac capillaries and quick death (HOPPE-SEYLER).

Under certain conditions the air passes back from out of the cavities abnormally filled with it into the blood, and with it also injurious substances, *e.g.*, sulphuretted hydrogen, from the intestine.

The DIAGNOSIS of emphysema depends in subcutaneous emphysema upon the presence of swelling and crepitation, in the accumulation of air in cavities, upon the clear, for the most part tympanitic percussion-note, and the displacement of neighboring organs, etc.

II. INFLAMMATION.

(*Inflammatio, Phlogosis.*)

VACCA, *De inflamm. morb. nat., causis, effect, et curat.*, 1765.—J. HUNTER, *On the Blood, Inflammation, and Gun-Shot Wounds*, 1793–1812.—BURNS, *Dissert. on Inflammation*, 1800.—RUST, *Helkologie*, 1811.—THOMSON, *Ueber Entzünd.*, transl. by Krukenberg, 2 Bde., 1820.—KALTENBRUNNER, *Exp. circa stat. sang. et vas. in inflamm.*, 1826.—GENDRIN, *Hist. anatomique des inflammations*, 1826.—BRÉTONNEAU,

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Des inflam. spéciales du tissue muqueux, et en particulier de la diphthérite, ou inflam. pelliculaire, connue sous le nom de croup, etc., 1826.—KOCH, *Meckel's Archiv,* 1832.— GLUGE, *Obs. noun. microsc. in inflamm.,* 1835.—GÜTERBOCK, *De pure et granulatione,* 1837.—RASORI, *Teoria della flogosi,* 2 vols., 1837.—VOGEL, *Ueber Ei'er, Eiterung, u. s. w.,* 1838; Art. "*Entzündung und Ausgänge,*" R. Wagner's *Handwörterbuch,* I., p. 311.—LEHMANN u. MESSERSCHMIDT, *Arch. f. phys. Heilk.,* 1842. I.—EMMERT, *Beitr. z. Path. u. Therapie,* 1842.—H. MÜLLER, *in Zeitschrift f. rationel. med.,* 1843, III.—BENNETT, *On Inflammation.* etc , 1844.—HENLE, in *Zeitschr. f. rat. med.,* 1844, II., p. 34; *Handb. der rat. Pathol.,* I. u. II.—LUSCHKA, *Entw. d. Formbestandtth. d. eiters u. d. granulationen,* 1845.—A WALLER, *in Phil. Magazine,* 1846, XXIX., pp. 271 an 1338.—Küss, *de la vascularité et de l'inflam.,* 1846.—HASSE, *Zeitschr. f. rat. Med.,* 1846, V.—BIDDER, *in idem.* 1846, IV., p. 353.—VIRCHOW, *in Virchow's Archiv.,* 1847, I., p. 272; IV., p. 261; XXIII., p. 415; XXIV., p. 205; *Annalen des Charité,* VIII., Hft. 3, p. 1; *Handb. der spec. Path.,* p 46.—BRÜCKE, *Sitzungsber. der Wiener Akad.,* 1849; *Archiv. f. phys. Heilk.,* 1850, X., p. 493.—PAGET, *Lectures on Inflam.,* 1850.—WHARTON JONES, *Guy's Hosp. Reports,* 1851, VII.—BECK, *Untersuchungen,* etc., 1852.—H. WEBER, *Müller's Arch'v.,* 1852, p. 361.—MECKEL, *Ann. des Charité,* 1853, IV., p. 218.—ROKITANSKY, *Sitzungsb. der Wiener Akad.,* 1854.—SCHÜLER, *Würzb. Verhandl.,* 1854, IV., p. 248.—SPIESS, *Zur Lehre v. d. Entzünd.,* 1854.—BONER, *Die Stase nach Exper. an der Froschschwimmhaut,* 1856.— SAMUEL, *Königsb. med. Jahrb.,* 1858, I.—GUNNING, *Archiv. f. holl. Beiträge,* 1858, I., p. 305.—SNELLEN, *Arch. f. holl. Beiträge,* 1858, I., p. 206.—O. WEBER, *Virchow's Arch ,* 1858, XIII., p. 74, XIX., p. 367; *Handb. der Chirurgie,* p. 362.—TREITZ, *Prager Vierteljahrschr,* 1859, IV.—COCCIUS, *Ueber d. Gewebe u. d. Entz. des menschl. Glasskörpers,* 1860.—SCHROEDER VAN DER KOLK, *Arch. f. holl. Beiträge,* 1860, II., p. 81.—J. SIMON, Art. *Inflammation* in *Holmes' System of Surgery,* I., 1860.—BUHL, *Sitzungsb. d. Bayr. Acad.,* 1863, p. 59; *Zeitschr. f. Biologie,* 1868, III., p. 341; *Lungenentzündung u. s. w.,* 1872.—E. WAGNER, *Arch. der Heilk.,* 1866, VII., p. 481; VIII., p. 419.—BILLROTH, *Arch. d. Chir.,* 1866, VI., p. 373.—COHNHEIM, *Virchow's Arch.,* 1867, XL., p. 1.—HELLER, *Ueb. d. fein. Vorg. bei d. Entzünd.,* 1869.—STRICKER, *Studien aus d. Inst. f. exper. Path.,* 1870, I.; *Oest. med. Jahrb. Jahrg.,* 1811 and 1872.
Consult also the literature of REPAIR ; and BILLROTH, *Surgical Pathol.* Am. Ed. ; Works on Practice of Medicine.

INFLAMMATION is a process, beginning for the most part with the phenomena of congestive hyperæmia, running its course most frequently with exudation or suppuration, sometimes healing, sometimes leading to new-formations, or to various kinds of metamorphosis, or to destruction of tissues, and causing a more or less marked disturbance of the function of parts. In certain cases sometimes all these changes are simultaneously present, sometimes only the first mentioned are found in a striking manner.

Inflammation RUNS ITS COURSE mostly as an acute, rarely as a chronic process.

Inflammation exhibits many TRANSITIONS: on the one hand, to many circulatory disturbances, especially to congestive hyperæmia and acute dropsy; on the other hand, to many disorders of nutrition, namely, to albuminous or fatty degeneration, to gangrene, as well as to new-formations, especially of connective and osseous tissues, and of vessels.

The name INFLAMMATION, and all terms to express it in other languages, point to a process connected with ELEVATION OF TEMPERATURE. But CELSUS proposed yet three other cardinal properties of inflammation, in all four: CALOR, RUBOR, TUMOR, DOLOR. Still another is added as a fifth symptom, FUNCTIONAL DISTURBANCE, thus designating all the phenomena of many processes as inflammation, especially of those running their course in the skin and visible mucous membranes.

Inflammation AFFECTS sometimes only one kind of tissue, especially among the simple tissues (connective tissue, serous membranes, periosteum, bones, epithelium, etc.), more rarely among tissues crowded together (interstitial, inter-muscular, inter-acinous, inter-lobular, etc., tissues), sometimes organs. In the latter relation it attacks sometimes only one tissue of a

compound organ (e.g., the glands of the mucous membranes, the gland-ducts, urinary tubules, acini of the glands, intestinal follicles, ovarian follicles, etc.), sometimes compound parts of an organ (lobes or lobules of the lungs), sometimes finally the organ in all its parts (e.g., the whole heart, whole gland).

Of organs in pairs inflammation affects sometimes only one of the pair (as in pleuritis, pneumonia, many forms of nephritis), sometimes both organs or parts of them (e.g., both cerebral hemispheres, both kidneys, both eyes, etc.); sometimes both relations are found (many pneumoniæ, inflammations of the parotid glands, etc.).

Inflammations of various tissues and organs are named mostly by adding to the Latin or Greek term, the ending -ITIS (e.g., encephalitis, pleuritis, nephritis, etc.); sometimes they receive special names, as pneumonia for inflammation of the lungs; erysipelas, etc., for inflammation of the skin, etc. Inflammations of the serous coverings of individual organs of the abdominal cavity are called PERI-hepatitis, perimetritis, etc. Peri-bronchitis, departing from this rule, is a term applied to inflammation of the outer halves of the bronchial wall. This is true also of peri-phlebitis, etc. Inflammations of the surrounding connective tissue, capsule, appendages, e.g. of the encasing fat of the kidneys, of the loose adipose and connective tissue of the lower and lateral parts of the urinary bladder, and of the uterus, are known as PARA-nephritis, para-cystitis, para-metritis.

The PROGRESS of INFLAMMATION takes place either in the continuity or in the contiguity of tissues, or upon distant lying organs and tissues. The progress of inflammation in the continuity affects sometimes the same tissues, sometimes those which are different from those first affected. The best known examples of the latter are when inflammation of the skin invades the bordering mucous membrane or vice versa, or when that of the bronchi invades the lungs (catarrhal, or lobular pneumonia), etc. Progress in the contiguity occurs most frequently in parts in contact with the skin, mucous membranes, serous membranes. Progress to distant tissues takes place either by means of the bloodvessels in a mechanical or chemical manner (embolism, pyæmia), or by means of the lymphatics, or in a sympathetic manner.

According to PFLEGER's (Med. Ctrlbl., 1872, No. 16; Arch. f. klin. Chir., XIV., p. 532) observations on the manner and laws of the extension of erysipelas migrans, those laws established by LANGER (Wien. acad. Sitzgsber., 1861 u. 1862, XLIV., p. 19) concerning the tendency to fissures and the tension of the cutis appear to come into question.

According to FEINBERG (Berl. klin. Wschr., 1871, Nos. 41–46), physiological and pathological facts show that myelitis can result from lesion of peripheral nerves, and that the results obtained in rabbits (laying bare and powerful cauterization of the sciatic: consecutive myelitis especially of the gray substance), also in man, tend to the same conclusion.

CAUSES OF INFLAMMATION.

The DISPOSITION TO INFLAMMATION is a general one. A series of factors and conditions, however, heightens the disposition as well generally as in inflammations of special organs. This is especially true of the various ages, of sex, as well as of a number of external causes, especially of atmospheric influences, soil, and climate (vide General Ætiology). Besides, influences of all kinds, which to healthy parts are harmless, are followed by inflammation in those whose vaso-motor nerves alone, or at the same time with the nerves of sensation and motion, are paralyzed (neurotic inflammations). Individuals who are tender, not hardy, badly nourished, scrofulous, rachitic and cachectic, convalescents, drinkers, are more subject to inflammations of the bronchi and lungs, etc. In some individuals some organs possess a

special predisposition to inflammation, in consequence of hereditary influence, etc. Repeated inflammation of many organs heightens the disposition to like affection of the same organ : e.g., repeated attacks of catarrh of most mucous membranes. Parts of organs are sometimes affected by inflammation more easily than other parts, from causes which are partly known, partly unknown. Inflammation of the lungs affects the upper lobes more often than the lower. Inflammation of the endocardium and of the heart belong oftener to the left ventricle ; the former occurs chiefly in the valves and openings, where the greatest tension and friction are.

THE IMMEDIATE, OR EXCITING CAUSES OF INFLAMMATION must vary in degree with the individual. The most prominent are : WOUNDS, as cuts, stabs, bruises—traumatic inflammations ; FOREIGN BODIES, as dust, splinters, gunshot ; many vegetable parasites ; worms or other parasites, wandering or fixed within the vessels ; accumulations of entire secreta in organs, as, e.g., the liver, the kidneys, the mammary glands, or of certain elements of them (e.g., biliary and renal calculi) ; emboli of every kind (p. 206), especially those acting chemically ; substances within serous cavities, and in other parts coming from hollow organs through perforations in their walls : the contents of the stomach and intestines, urine, especially if of an alkaline reaction, etc. ; gangrenous parts of the body even (limiting inflammation) ;—HIGH DEGREES OF HEAT AND COLD, as well as also "catching cold" (p. 61) ; CHEMICAL influences, as of acids, alkalies, ethereal oils, cantharides, mustard, tincture of iodine, stings of insects, etc. ; alcohol by habitual use.

Many of the known exciting causes act upon the deep tissues : the most important in this respect is the pneumonia arising from the presence of foreign bodies.

THE INFLUENCE OF THE NERVES upon the origin of inflammation has been demonstrated with sufficient certainty, in part experimentally, in part by clinical and pathologico-anatomical observations. After section of the n. trigeminus or of its ophthalmic branch, or only of the internal fibres of the latter within the cranial cavity, there arise, soonest to the extent of the inflammation, peculiar disturbances of nutrition of the conjunctiva and cornea, and, for the most part also, of the surrounding skin. Casual wounds or diseases of these nerves, or of the Gasserian ganglion, have been followed by the same results. After traumatic or other inflammations, new-formations, etc., of these nerves, or of a spinal ganglion, or of the nerves passing through it, there have been observed in many accurately investigated cases peculiar inflammations of the skin of the character of herpes, to wit, herpes zoster. After like causes, also, repeated disturbances have been observed which are not to be clearly ranked with inflammations, but as transitions to dropsy, gangrene, atrophy, and hypertrophy.

The physiological experiments in this connection are those of MAGENDIE. LONGET, VALENTIN, SCHIFF, BERNARD, SNELLEN, BÜTTNER, MEISSNER, and others. For cases of inflammation with serous exudation, see : ROMBERG, *Klin. Ergebn.*, 1846, p. 4 ; the Author, *Arch. d. Heilk.*, 1870, XI., p. 319. Cases of sero-purulent inflammation, especially herpes of the skin, are described by RAYER, DANIELSSEN ; particularly BÄRENSPRUNG, *Ann. d. Char.*, 1861, IX , 2 H., p. 119 ; *Ib.*, XI., 2 H., p. 100 ; GERHARDT, *Jen. Ztschr.*, 1865, II., p. 349 ; the Author, l. c., p. 320 ; WEIDNER, *Berl. klin. Wschr.*, 1870, No. 7 ; WYSS, *Arch. d. Heilk.*, XII., p. 261. Also cases by DE HAEN, ESMARCH, DUNCAN, VERNON, GREENOUGH, EULENBERG-LANDOIS, EULENBERG, GUTTMANN, HORNER, HUTCHINSON, and others. More recently BROWN-SÉQUARD (1861) has again turned attention to the frequency of subacute and chronic inflammations of the joints of paralyzed extremities.*

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* For an account of the joint-lesion occurring in paralytics, consult, CHARCOT, *Arch. de physiol. norm. et path.* I. p. 161, p. 379 ; *Leçons sur les maladies du syst. nerveux,* Paris, 1873, p. 105, et seq. B. BALL, *Med. Times and Gazette*, Lond. 1868-9. S. W. MITCHELL, *Injuries of Nerves*, Phil. 1872, p. 168. [ED.]

Sometimes also the influence of the nerves in giving rise to inflammation is REFLEX in character. SCHIFF often observed in dogs, whose lingual nerve only, or inferior dental nerve, he had cut, after four to eight days' injection of the conjunctiva of the eye of the same side, increased secretion of mucus and a partial gray cloudiness of the cornea, which after about twelve days again disappeared, as if an affection of the vaso-motor nerve of the n. ophthalmicus. In like manner must those observations be explained, where, after wounds and operations on the upper maxilla and its nerves, there appeared in the eye of the same side, with normal sensibility, injection of the conjunctiva, cloudiness of the cornea, softening, ulceration and perforation of the centre, with consequent staphyloma and atrophy. (A. WAGNER, *Arch. f. klin. Chir.*, 1869, XI., p. 1.)

Injurious substances, which have their origin in the same or another organism, may be carried directly by the blood or by the lymph out of the organs as excitants of inflammation : those of the fixed contagions belonging to this class are the mucus of gonorrhœa, the syphilitic virus, the pyæmic poison, the contagium of dysentery, of hospital gangrene, of many conjunctival catarrhs, of glanders; those of the volatile contagions especially to be mentioned are, that of influenza (epidemic bronchial, and intestinal catarrh), the contagium of typhus and typhoid fevers, of scarlatina and small-pox. In many of these cases lower forms of fungi probably play an important rôle (p. 102).

PHENOMENA OF INFLAMMATION.

EXPERIMENTALLY PRODUCED.

The PHENOMENA of inflammation are to be followed in tissues and organs of every kind in the dead body as well as in the external parts (skin, externally visible mucous membranes, especially the membranes of the eye) during life. But far greater disclosures are made by EXPERIMENT, and the simultaneous continuous and immediate observation for hours and days of inflamed parts under the microscope.

Corrosive substances (particularly ammonia, nitrate of silver, acids and the like), strong irritants (alcohol, tincture of cantharides, mustard, etc.), as well as substances with strong diffusive power (salt, chloride of calcium, etc.), have been applied EXPERIMENTALLY to parts of known structure and which are transparent and easily to be observed, as the web of the frog, the wing of the bat, the cornea, the tongue and the mesentery of the frog and of mammals, etc. Or, without farther preparation the internal organs have been subjected to observation, since the access of air is usually a sufficiently strong excitant of inflammation. Like the effects of these substances are those of wounds with needles, transfixion by threads, etc., high degrees of heat and cold. Thereafter the following is in general to be observed. Numerous differences which cannot be explained are caused by the kind of materials employed, especially if they act only in a diffusive manner (chloride of sodium, etc.), or at the time as irritants (spirituous and corrosive substances, etc.).

If a VASCULAR ORGAN, *e.g.* the mesentery or tongue of the frog, be examined under the microscope, there is observed, first a uniform DILATATION OF THE ARTERIES, which after about two hours reaches its highest point and may double the original diameter of the vessels; besides, their length becomes considerably increased. DILATATION OF THE VEINS follows much more slowly, reaching the same degree as in the arteries without an increase in their length. The VELOCITY OF THE CURRENT at first constant, is, after a few hours, DIMINISHED : the individual blood-corpuscles can be distinguished. Pulsation is observed in the arteries. The blood-stream in the arteries and

veins has lost its axial character (present under normal conditions): the blood fills the whole calibre of the vessels. Now, within the veins the peripheral zone of the blood-stream, the original plasma stratum, becomes gradually FILLED with innumerable COLORLESS BLOOD-CORPUSCLES. At first single corpuscles, then more and more, come to a standstill, so that after a certain time the whole inner surface of the veins appears lined with a uniform layer of such corpuscles, while within this layer the red blood-stream flows uniformly on. Again, after a certain time COLORLESS BLOOD-CORPUSCLES are observed TO PASS OUT from the interior of the veins THROUGH THE UNINJURED WALL OF THE VESSELS: upon the exterior of the veins are formed small, colorless, knob-like elevations, which slowly increase in size, still connected with the wall of the veins, but finally separate from it and wander farther and farther from the veins into the surrounding tissue. During this time new colorless corpuscles separate from the blood-stream to the inner wall of the vein, and then pass through the wall. This process is accomplished sometimes within half an hour, sometimes only after many hours—the time varying with the vein and with the animal. IT IS THE SAME ALSO WITH COLORLESS BLOOD-CORPUSCLES, WHICH HAVE PREVIOUSLY BEEN IMPREGNATED WITH ANILINE BLUE, CINNABAR, etc. Simultaneously with the larger vessels, THE CAPILLARIES also are DILATED, for the most part only from a sixth to a fourth. In one part of them the blood stream flows on continuously, and with uniform velocity. In another part, it is entirely or partially arrested: the colorless corpuscles show amœboid movements and, as in the veins, pass out in the same manner through the vessel-wall. Besides, RED GLOBULES also pass OUTWARD THROUGH THE VESSEL-WALL; they squeeze through the wall with greater or less difficulty, and sometimes appear on the outside entire, sometimes only in part, while the other part is torn away by the blood-current. Thus after a few to 24 hours the capillaries are seen to be surrounded by numerous corpuscles, of which the greater number are colorless, the fewer colored corpuscles; the latter entire or in fragments.

DILATATION of the large vessels depends upon a paralysis of their muscles: the latter may be direct (influence of the air), or reflex (through sensory nerve fibres). The RETARDATION of the blood current is due to the increase in size of the stream. The ACCUMULATION OF COLORLESS BLOOD-CORPUSCLES IN THE ZONE NEAREST THE VESSEL-WALL is in consequence of the diminished velocity of the stream: this is greater in the axis of the vessel than in the periphery (DONDERS and GUNNING); the colorless corpuscles are moved along not merely in the direction of the stream, but also are revolved about their axis, and through both circumstances they come to the periphery (COHNHEIM). According to others, it is the glutinosity of the colorless corpuscles, by virtue of which they, once brought in contact with the vessel-wall or with one another, immediately adhere, and this adhesion is in direct ratio with the slowness of the stream: the cause of the glutinosity lies in the fine processes, which the cells invariably have also during their onward flow. (HERING, Wien. Acad.-Ber., 1868, LVII., p. 170.)

THE FORCE UNDER WHICH THE BLOOD-CORPUSCLES PASS OUT OF THE VESSELS, is different for each kind. The colorless blood-corpuscles should, so long as they continue within the uninterrupted current, always preserve the spherical form; as soon, on the other hand, as they become quiet, amœboid movements appear in them, they push out their processes against those parts of the vessel-wall where they meet with the least or no resistance, i.e., toward the stomata and open spaces of the connective tissue. While the colorless blood-corpuscles thus actively pass out of the vessels, the chief force in the passage outward of the red corpuscles is the increased blood-pressure (COHNHEIM). According to HERING, the exit of the colorless corpuscles through the uninjured vessel-wall is chiefly a consequence of the blood-pressure and current velocity. H. regards the exit as a simple filtration of colloid substances: he found that colored glue, even under comparatively low pressure, if it only lasted long

enough, filtered through the vessel-wall.—Also SCHKLAREWSKY (*Arch. f. d. ges. Phys.*, 1868, I., pp. 603 et 657) conceives the wandering outward of the blood-corpuscles to be purely physical. (See also p. 152.)

Concerning the WAY BY WHICH the blood-corpuscles pass out of the vessels, see page 152-3.

The blood-corpuscles which have wandered out of the vessels remain only a short time in the immediate neighborhood of the vessels, but continue to move farther away from them, and are replaced by more recently migrated corpuscles. After a few hours the mesentery is filled with them in varying quantity. The red corpuscles remain in the immediate neighborhood of the capillaries, unless they are removed from them by increased transudation or by other forces. Besides, there can be seen the basement membrane of the mesentery, or of the mucous membrane of the tongue, the nuclei of the epithelia, and the connective tissue corpuscles in the same places, with the same form and with the same distinctness, as far as they are not concealed by the migrated blood-corpuscles. The wandering corpuscles REMAIN IN PART WITHIN THE TISSUES of the mesentery or of the tongue, IN PART THEY COME TO THEIR SURFACE: the latter, either directly, or after they had first traveled a greater or less distance. Simultaneously, THERE EXUDES FROM THE VESSELS AN ABUNDANT PLASMA, which soon coagulates and thereby incloses the migrated corpuscles.

The phenomena are the same also when an irritating substance has been introduced into the peritoneal cavity of the frog, and from time to time the intestine is drawn out and examined microscopically. These observations have been corroborated also in warm-blooded animals. Most probably the process in most other organs differs only in that the greater number of the white blood-corpuscles come from out of the capillaries (and not, as in the mesentery which is poor in capillaries, from out of the veins), and then for the most part also large numbers of red corpuscles pass out of the vessels.

Against the view, that in large suppurations the whole mass of pus-corpuscles cannot be colorless blood-corpuscles, is briefly answered, that the number of white blood-corpuscles in the circulation is usually underrated, since many more are found in the small veins and capillaries than in the large vessels and heart. Besides, during the existence of inflammatory processes, the spleen, lymphatic glands, etc., become hyperplasic, and thus provide a constant renewal of colorless corpuscles (CONNHEIM). As far as possible the swelling of the lymph-glands is, however, not to be received in this sense, but the cells found in the lymph-glands of inflamed parts must perhaps likewise be regarded as migrated cells (HERING). In the latter case the mode of increase of the colorless blood-corpuscles, at least in large suppurative inflammations, is still obscure. According to SCHIFF (*Speech in the Acad. of Sciences*, Florence, June, 1871), in large formations of pus, the very great number of pus-corpuscles proceed from an irritation of the internal vessel-wall, as it were a catarrh of its epithelium.

In NON-VASCULAR TISSUES (cornea, etc.) THE PUS-CORPUSCLES ALL IN LIKE MANNER HAVE THEIR ORIGIN IN THE VESSELS OF THE NEIGHBORING TISSUES. If the cornea be cauterized with nitrate of silver, there will be formed an opaque, grayish-white spot, which after a short time becomes brown. If the cornea be transfixed by a silk thread, there will be formed around it a small whitish circle, which is a consequence of small radiating fissures into the corneal tissue, into which the aqueous humor finds its way. Farther on, however, there is formed on the border of the cornea (not, as others assume, in its centre or around the irritated parts), a gray cloudiness, which advances in the shape of a wedge towards the thread: it is dependent upon

the migratory colorless blood-corpuscles (pus-corpuscles), which have accumulated in varying number and form in the tissue-spaces NEAR the corneal corpuscles. A part of these will contain coloring matter if it has previously been introduced into the blood of the animal. Even an examination with the naked eye, still more that under the microscope, demonstrates that the pus-corpuscles have their origin within the vessels of the corneal border.

Inflammation in vascular as well as in non-vascular parts either RETROGRADES, or is followed by OTHER PROCESSES. In the former case not only the transuded plasma is reabsorbed, but also the migrated colorless bloodcorpuscles disappear, because they can pass out of the connective-tissue spaces into the lymphatic vessels, and thence again into the blood.

If substances (wadding—tincture of cantharides, lunar caustic), acting as mechanical or chemical irritants, be introduced into the cavity of the abdomen of a frog. or if the intestine together with the mesentery be drawn out of the abdominal cavity and exposed to the air, there will be developed a peritoneal inflammation, with FIBRINO-PURULENT EXUDATION. In the first place, a hyperæmia quite suddenly appears. After a few hours the serous membrane is covered with only a thin, but gradually thickening, cloudy, removable substance, the exudation, under which the vessels can only be indistinctly recognized. After twelve to twenty-four hours the exudation is thicker, soft, dull-gray or yellowish, and removable in larger or smaller shreds. They consist, under the microscope, of compact pus-corpuscles, single red blood-corpuscles, and an intermediate amorphous or faintly granular substance, made clear by acetic acid.

According to what has just been stated, the ESSENTIAL PHENOMENA OF ACUTE INFLAMMATION are thus congestive HYPERÆMIA of the vessels, EXUDATION OF SERUM AND FIBRIN, the EXIT OF RED, BUT ESPECIALLY OF COLORLESS BLOOD-CORPUSCLES. The latter form the pus-corpuscles.

In opposition to this view there is another older, according to which the PUS-CORPUSCLES are not the migrated colorless blood-corpuscles, but have their origin IN THE TISSUES THEMSELVES. In epithelial tissues the epithelial or gland-cells, in connective tissue organs of every kind the connective tissue and analogous corpuscles, are the foci of growth of the pus-corpuscles : by single or multiple division, by endogenous cell-formation, etc. This theory is also in great part supported by experiments, particularly on non-vascular parts. But no immediate observations of inflamed parts were originated and continued during the life of the animal, and the colorless blood corpuscles by absorption of coloring matter had not been made recognizable, and were thus distinguished from pus-corpuscles which may have been newly formed. Only recently have direct observations made this mode of suppuration again more probable. Besides, the theory has just been brought forward, that in inflammation not only the migratory connective tissue corpuscles can become pus-corpuscles, but that also fixed cells can become completely migratory.

From the foregoing it follows. that the point in dispute in the doctrine of inflammation is chiefly. the genesis of pus-corpuscles. The oldest theory, that the puscorpuscles had a free origin in a structureless exudation, has been for a long time entirely abandoned. After this followed almost two decades, during which the theory prevailed, that pus-corpuscles had their origin in the tissues themselves. The latter theory was first taught by VIRCHOW and his pupils (STRUBE), by His and others; but after the more recent demonstrations by COHNHEIM given above, it can no longer, or only in part. be maintained. Still earlier indeed had DÖLLINGER (1819), J. MÜLLER (1824), KOCH. and HASSALL observed a migration of the colorless blood-corpuscles from out of the vessels and these were pronounced by KALTENBRUNNER (l. c., 1826), ADDISON (*Consumpt. and Scrof.*, 1849, p. 82), and ZIMMER-

MANN (*Preuss. Vereinszeit.*, 1852, p. 64, 144 u. 239) to be identical with pus-corpuscles. But A. WALLER (l. c.) first described in 1846 the phenomenon in the frog's tongue more exactly, and insisted upon the identity of the two kinds of corpuscles, and of the processes which concern them. In the years which followed, WALLER's observations were so entirely forgotten that COHNHEIM's description was immediately regarded as representing a discovery.

At present these two theories concerning the origin of the pus-corpuscles are sharply opposed to each other : the one, that all pus-corpuscles are migrated colorless blood-corpuscles ; the other, that only a part of the pus-corpuscles have this origin, but that the other part arises by one of the above described methods from the original tissue-cells. The majority range themselves on the side of the MIGRATION THEORY, which experimentally it is comparatively easy to understand, and with which harmonize most of the forms found in dead human and animal tissues. But the other also, the PROLIFERATION THEORY, is held by many of the best investigators. Below we furnish a number of the arguments adduced by both sides, of which the most and best had their origin in the examination of the cornea. Below also many other facts will be considered.

If the cornea be wounded in or near the middle of it, by passing a thread through it, by cauterization, etc., there will follow, according to the older theory of VIRCHOW and his pupils, HIS and others, a cloudiness of the corneal cells with albuminous masses, and an enlargement of them. If the affection be slight, the changes are arrested at this stage, and a *restitutio in integrum* follows. At other times, however, other processes follow. Immediately there appears an increase of the elements. The nucleus of the connective-tissue corpuscles enlarges and divides ; division of the cell follows that of the nucleus, and very soon the place of the single cell is occupied by a brood of new cells. The production of cells proceeds so incessantly, that the original tissue is soon destroyed, and in its place are found only round, young cells, with albuminous inter-cellular fluid : pus-formation. While this takes place in non-vascular parts, which the irritant only has affected, there follow in the neighboring capillaries similar expansion and over-filling of the blood, as in other parts which are vascular, and where the irritant affects the vessels directly. According to VIRCHOW's theory, the increase in size, cloudiness, and growth of the cells are the first things observed after the action of the irritant ; these processes appear earlier than dilatation and determination of the blood in the nearest bordering vessels.

The results of the altogether different experiments of COHNHEIM are given in full above.

COHNHEIM's views have been confirmed on many sides, at first by KREMIANSKY (*Wien. med. Wschr.*, 1868, Nos. 1–6). K. found after cauterization of the cornea, before the appearance of cloudiness at the periphery, an accumulation of pus-corpuscles about the point of irritation : this, according to him, is the result of the migration of the connective-tissue corpuscles to the place of irritation ; the colorless corpuscles (recognizable by the cinnabar with which they had been colored) arrive at the same point only after two to four hours. An observation by EBERTH is equally important. A majority of frogs in winter are affected by melanæmia. If a corneal inflammation be induced in them by separation of the epithelium, there will be observed after a little time in the corneal tissue, by the side of the colorless amœboid cells, a not inconsiderable number of those which are filled with black, finely-granular pigment, and possessing equally active movements with the former. Also black pus has been found in the mesentery. (*Virch. Arch.*, 1870, LI., p. 145.)

Among the most prominent of the opponents of COHNHEIM's theory, stand RECKLINGHAUSEN and STRICKER.

HOFFMANN and RECKLINGHAUSEN (*Med. Ctrlbl.*, 1867, No. 31) found in the hollow spaces of an excised cornea of the frog or cat—after it had been cauterized in the centre, and preserved a day and longer under suitable conditions—a so considerable number of pus-corpuscles, that they assume their formation from the MIGRATORY corneal corpuscles. HOFFMANN (*Virch. Arch.*, XLII., p. 204) has seen in such corneæ the migratory cells accumulate about the point of irritation : in the frog in forty-eight hours, in the rabbit in twenty-four. In the immediate zone around the injury, the stellate cells of the cornea were unchanged ; then followed a ring which consisted almost entirely of only rounded movable forms, sometimes so numerous, that the new-formation of cells was not to be doubted. Here the fixed or stellate cells had almost entirely disappeared.

COHNHEIM (*Virch. Arch.*, 1869, XLV., p. 333) has refuted these statements. He saw during observation of superficial wounds on the tip of the tongue without loss of blood, the fixed connective tissue corpuscles assuming many forms, either pale and finely granular, or coarsely granular. Near the wounds they were transformed into

finely granular globules, similar to corneal cells. Simultaneously, there arose a dilatation of the vessels; the red blood-corpuscles migrated through the capillaries, the white chiefly through the veins. Nowhere was there shown a proliferation of the connective-tissue corpuscles. Thus also in healing by granulation, at least at the beginning of suppuration, the source of the pus-corpuscles is demonstrated. Moreover, COHNHEIM has in frogs supplied the blood with a solution (0.75 per cent.) of common salt, and induced in them a traumatic keratitis. The corneæ remained clear, the stellate corneal corpuscles did not show the formation of pus.

Recently, STRICKER has declared himself opposed to the universal prevalence of the WALLER-COHNHEIM theory, by experiment and inference. According to STRICKER, pus-corpuscles arise in various epithelia partly by division, partly by endogenous formation, from connective-tissue corpuscles, from muscular cells, &c. Besides, according to STRICKER, in the inflammatory process, fixed cells (many epithelia, branched corneal cells, cells of the capillary walls) become migratory not only to a certain degree, but even entirely so. Finally STRICKER has also seen a migratory cell transformed into two independent migratory forms.

NORRIS and STRICKER (*Stud.*, 1870) describe, in opposition to COHNHEIM, a doubtless considerable nuclear increase in the inflamed cornea of the frog; they hold that the MULTINUCLEAR MIGRATORY MASSES HAVE THEIR ORIGIN IN THE FIXED CORNEAL CORPUSCLES. The nuclei of Descemet's epithelium also are increased in number.

According to STRICKER (*Ib.*, p. 18) THE MIGRATORY CELLS OR PUS-CORPUSCLES IN INFLAMMATION INCREASE BY DIVISION. (S. experimented on the tongue and cornea of the frog.) Increase of pus-corpuscles in mass could not previously be shown; it is not to be distinguished also from a passing accumulation of liquid. By examination for one hour of the mucous membrane of a frog's tongue partly torn off on the day before, it was shown that even the apparently fixed connective-tissue corpuscles assumed a certain degree of mobility in the process of inflammation; that in them there were observed appearances, which pointed to attempts at division; that parts of them became movable as though they were only amœboid cells. Upon the whole, STRICKER believes that a sharp line is not to be drawn between migratory and fixed connective-tissue corpuscles. Finally, STRICKER observed, that a bi-nu clear cell of Descemet's epithelium can divide into two migratory cells (or pus-corpuscles), as well as that the larger poly-nucleated and more inactive elements of the inflamed cornea may become wholly or in part like the migratory cells in appearance and movements.

OSER (*Ib.*, p. 74) also holds to the endogenous formation of cells: according to his observations the endogenously formed pus-corpuscle is born in the conjunctiva of the rabbit like a young trout; it leaves by amœboid movements the vesicular space in the interior of the epithelial cell. (Consult also HANSEN, *Wien. med. Jahrb.*, 1871, p. 210.)

KREMIANSKY cauterized the ensiform process of hens (the skin being immediately closed over the cartilage), and found, eight to ten days afterward, pus-corpuscles containing cinnabar, only about the cartilage, never within it; whereas in the cartilage immediately adjacent to the necrotic portion there was an increase of cartilage-cells (ten to thirty) within the capsules, resulting at the end in the formation of cells, which were entirely analogous to pus-corpuscles.

According to DURANTE (*Wien. med. Jahrb.*, 1871, p. 321), in inflammations of the vein-wall, endothelium, muscular cells, and connective tissue nuclei participate in the proliferation. The intima shows first an irregularly distributed increase of inter-cellular substance; later, the inter-cellular substance increases in the whole periphery of the endothelial cells, these even become oval or round, the body of the cell becomes granular, the nuclei show marks of division: two, four, six, eight of them appearing in one cell. The cells now show either OSER's endogenous cell-formation; or the cleft nuclei crowd against the periphery of the cells. Small elevations, buds, make their appearance, in which, during the gradual separation, the nucleus remains inclosed: finally, there are to be observed in the midst of the inter-cellular substance a great number of such cells, whose origin is by gemmation, or at least by a process bordering upon it. The changes in the adventitia are not to be distinguished from those of common connective tissue in inflammation. The connective-tissue cells swell, and assume an oval, round, or irregular shape; later, their nucleus divides into two, three, or more parts, which is afterwards followed by a division of the cells themselves. The smooth muscle-fibres show a proliferation of their nuclei and division of the spindle cells themselves into smaller segments. The endothelia of serous membranes (KUNDRAT, *Ib.*, p. 226), bone-corpuscles (LANG, *Ib.*, p. 34. RUSTIZKY, *Ib.*), cartilage-cells (HUTOB, *Ib.*, p. 398), behave in a like man-

ner. Consult also HEITZMANN'S (*Ib.*, 1872, pp. 339—357) experimental investigations on inflammation of bone and cartilage.

KLEIN and BURDON-SANDERSON (*Med. Ctrbl.*, 1872, Nos. 2–4) observed in rabbits and guinea-pigs, on the inflamed peritoneal side of the diaphragm, that the endothelial cells put forth buds which became separate as young amœboid cells. Similar observations have been made by us on the pleural side of the diaphragm, on the mediastinum and omentum. In chronic inflammations there are observed, especially in the true stomata, oval, bud, and cone-shaped swellings, which consist of proliferating endothelial cells.

Two important works on this subject again support COHNHEIM. The first of these is the more important, in that it at the same time regards the latest investigations of RANVIER and SCHWEIGGER SEIDEL respecting connective-tissue and corneal corpuscles.

A. KEY and C. WALLIS (*Nord. med. Ark.*, 1871, III, No. 16; *Virch. Arch.*, 1872, LV., p. 296) cauterized the cornea some seconds with the point of a stick of nitrate of silver. Around this point vacuoles were formed at first in the nuclei, not in the protoplasm of the corneal corpuscles, later in the latter also and in the vacuole-zone, whereby they were finally destroyed. In the frog this destruction has mostly appeared before a single new-formed or immigrated cell has appeared in the vacuole-zone. (The formation of the vacuole-zone and the destruction of the corneal corpuscles are results of the destructive influence of the silver salt; they are wanting in mechanical irritations of the cornea, *e.g.*, after the passing through of a thread.) Around the vacuole-zone the corneal corpuscles are unchanged. In frogs the migration of cells from the periphery of the cornea toward the centre first begins on the second or third day, earlier and in greater numbers in the anterior lamellæ than in the posterior. Only at the end of the first or beginning of the second week have they reached the cauterized point, later they wander into the slough. They are always most numerous in the innermost parts of the vacuole-zone. Then the corneal corpuscles beyond the vacuole-zone are besides unchanged: they show no trace of division of the nucleus, etc.; near them, in the same space of the basis substance, lie the migrated cells. The latter differ much in size and form, having from one to twelve nuclei; varying in size from one to tenfold; in shape smooth and unstable, or spindle-shaped, etc.; but motion and migration are common to all, as well as the presence of cinnabar when this substance had been injected into a lymph-space. In frogs in summer the processes are essentially the same, but are much more rapid, and the number of migrating cells is greater; besides, red blood-corpuscles also are found.

F. A. HOFFMANN (*Virch. Arch.*, 1872, LIV., p. 506) observed the following: After injections of cinnabar, even in very large quantities, granules of cinnabar are always sparingly found in the fixed cells of connective tissue. But if at any point an irritation is produced (in rabbits by cauterization with nitrate of silver or by injection of acetic acid under the skin) here the cinnabar accumulates in very considerable quantity. After four weeks, pus from such points was always free from cinnabar, notwithstanding that the tissues secreting this pus still included cells bearing cinnabar in large quantity. This goes to show that the connective tissue corpuscles are altogether passive in the formation of pus.

According to RANVIER (*Nouv. dict. de médec. et de chir. prat.*, 1870. XIII., p. 675), the laminated pavement epithelium of serous membranes, bloodvessels and lymphatics, of the alveoli of the lungs and glomeruli of the kidneys, as well as the flat cells of connective tissue, under the influence of inflammation return to the embryonic state, and after the disappearance of the inflammation, these embryonic cells again form the original tissue. In artificial peritonitis the endothelial cells at first swell up, become granular, their smooth nuclei become spherical and then divide, then the cells having become globular also divide. Many of them become completely separated from the basement membrane, fall into the peritoneal cavity, and mingle with the numerous migrated white blood-corpuscles. If the inflammation recedes, these free cells become fixed, unite with the white blood-corpuscles, upon the surface of the serous membranes spread out laterally, and form anew a complete epithelial covering. It happens thus also in fibrinous pneumonia. The endothelia, which form the capillary wall, act in a similar manner in inflammation: thus is explained the passage outward of white blood corpuscles through the capillary walls.

FLEMMING (*Virch. Arch.*, 1872. LVI., p. 146) induced artificially (by threads, iodine, croton oil) inflammation in the subcutaneous connective tissue of rabbits and dogs. The fixed connective-tissue cells show no processes of increase, or only rarely. But such separate forms are not wanting even in healthy connective tissue, and are frequently met with in localities where there is a forming of fat and in fœtal tissue. On the other hand, F. found double or numerous nucleoli, often of very large size,

oftener than in normal tissue. Here and there where pus is being formed, in place of the delicate, flat connective tissue corpuscles, there are found thicker, compact, smooth-walled corpuscles, flat, spindle-shaped, or branched; or round, spindle-shaped corpuscles, connected more firmly to one another by thicker anastomoses. The cellular elements, under the influence of inflammation, return to the embryonic type : RANVIER. In inflamed tissues the substance of a cellular plane may be retransformed into the much moister, more compact form of an embryonal connective-tissue cell. All these states correspond with the cloudy swelling of VIRCHOW. In many preparations the cells thus changed in the non-vascular vicinity of a fat-lobule are filled with small and medium-sized oil-globules. In only one case in seven, after irritation by croton oil, was there shown a proliferation of fixed cells, but which in no probability led to the local production of pus.

According to KÖSTER (*Virch. Arch.*, 1872, LV., p 455), the pigmented connective-tissue cells during inflammation of the lungs become migratory, and appear with their pigment in the alveoli.

GÜTERBOCK (*Virch. Arch.*, 1872, LVI., p. 352), after incomplete tenotomy of the *tendo Achillis* of rats, found no inflammatory changes in the elements of the tendon. The funnel-shaped space of the wound becomes almost completely filled by the ensheathing tissue ; this contains young cells, nuclear divisions of the endothelia.

Also BIZZOZERO'S (*Oestr. Jahrb.*, 1872, II., p. 160) clinical observations, and his experiments on the exciting of hypopyon, do not support free cell-formation: the large mother-cells with the daughter-cells (ten to twenty in number) have their origin in the swallowing up of pus-corpuscles (also red blood-globules) by the epithelium of the parts in question.

PATHOLOGICAL ANATOMY, AND PATHOLOGY.

THE FOUR PRINCIPAL PHENOMENA OF INFLAMMATION, therefore, are : HYPERÆMIA, EXUDATION WITH SUPPURATION, NEW-FORMATION OF TISSUES, AND THEIR TRANSFORMATION OR DESTRUCTION.

These principal phenomena are not always present. They are purest, especially hyperæmia and exudation with or without suppuration, in ACUTE inflammations, which run a quick course within a few days or weeks, and terminate either in resolution (*i.e.*, healing), or in suppuration or mortification, the causes of which act quickly, and are quickly removed, or disappear spontaneously. In CHRONIC inflammations, on the other hand, the causative force is found to be an irritation, acting not once but repeatedly; or the irritant is not removed ; or it consists especially in predispositions to inflammation. In all such cases hyperæmia of the capillaries is sometimes slight, sometimes it is more marked ; serous exudation is for the most part considerable ; also the formation of mucus is often considerable and particularly of long duration ; suppuration may be wanting or of trifling amount. The tissues sometimes become atrophic or flaccid, destitute of elasticity ; sometimes there is found a new-formation of tissues, particularly of connective tissue and of osseous tissue. Connective tissue is not infrequently so abundant that by it the remaining tissues (gland-cells, nerve- and muscle-fibres) are destroyed : inflammatory induration.

THE FIRST PRINCIPAL PHENOMENON OF INFLAMMATION IS CONGESTIVE HYPERÆMIA.

Hyperæmia—according to what is found in dead bodies—shows several grades : sometimes simple accumulation of red and especially of white blood-corpuscles in the capillaries without co-existent changes ; sometimes, besides, uniform or irregular dilatation and elongation of the capillaries, and such close crowding together of the red corpuscles that the contours of single ones cannot be distinguished.

Hyperæmia, however, is not the whole of inflammation, but it must be present if the process is to be designated as inflammatory. For, in the first

place, hyperæmia explains the redness of the part, also its increased warmth and a part of the swelling. In the second place, we must include in inflammations also the alterations of nutrition, which in non-vascular parts appear after the operation of the same irritant, because the changes included therein are quite the same as in vascular parts. These non-vascular parts are, besides the cornea and cartilage, all membranes in their epithelial covering, especially if the latter is made up of many laminæ : here the nearest vessels, namely those of the papillæ of the corium of the skin or mucous membranes, are the seat of the hyperæmia. In the third place, finally, hyperæmia and elevation of temperature may exist locally without inflammation, as is shown in the neck after section of the sympathetic.

Hyperæmia, however, is a necessary phenomenon of inflammation. It determines in general, in many cases, the height of the inflammation. In external parts, as the skin and bordering mucous membranes, it is an especially valuable symptom of inflammation : for here it is never absent. It varies in shade of color from the palest to the darkest red, which depends partly upon the severity, partly upon the cause and character of the inflammation, partly upon conditions which are unknown. For the most part, the redness in the middle of the inflamed part is darker, and toward the periphery assumes a lighter shade. It is sometimes uniform, sometimes spotted, sometimes streaked, etc.

As in common congestive hyperæmia, so also in inflammation, is the circulation ACCELERATED. But during the progress of the inflammation, especially if of long duration, after exudation, etc., it is RETARDED.

SAMUEL (*Virch. Arch.*, LI., pp. 41–178) has carried on experiments on the influence of ligation of arteries upon the origin and course of the inflammatory process : that influence is only exceptional, and to a slight extent perceptible.

How overfilling of the blood in a few vessels under the operation of irritating causes so quickly occurs, sometimes, after a previous contraction of the small arteries, is not yet made clear. Three different explanations (theories of inflammation) are offered.

The CONTRACTION which has often been observed in the smallest arterial vessels in the beginning of inflammation, is explained by the convulsive contraction of their muscles, which, as is known, are strongly developed precisely in the smallest vessels. Also in the capillaries independent contraction and dilatation have been observed.

Of the three THEORIES OF INFLAMMATION, each is to a certain extent intelligible, but no one wholly so.

According to the SPASMODIC THEORY, the accumulation of blood depends upon a cramp of the smallest arteries or veins. This is produced by the irritant in the same place and point, or it is reflex in origin through the irritation of a cooling of the skin, etc. (CULLEN, EISENMANN, BRÜCKE). This theory is untenable, because it does not explain all inflammations : *e.g.*, those caused directly by warmth, those arising from an interruption of the venous current.

According to the PARALYTIC THEORY (VACCA, WILSON, HASTINGS, STILLING), the irritation affects only the sensory nerves, *e.g.* of the skin, and produces an antagonistic paralysis in the vaso-motor nerves. The vessels then, in consequence of the paralysis of their nerves, relax, dilate, and receive more blood. It is opposed to this theory, that retardation of the blood depends only upon partial dilatation of the arteries, while uniform dilatations of them by reducing the friction accelerate the blood-current.

According to the ATTRACTION-THEORY (HALLER, LANGENBECK, EMMERT, J. VOGEL), or the assumption of a NUTRITIVE IRRITATION (VIRCHOW), an increased attraction between the parenchyma of organs and the blood is the cause of the slower movement of the blood. Or, according to VIRCHOW, it is the cell in itself, without the intervention of the nerves and of the blood, which is excited to increased nutritive activity, to greater metamorphosis, and to new-formation ; and the more quickly this

takes place, the more it runs the danger even of destruction, the more is the process to be looked upon as inflammatory. In support of this view it is asserted that from the experiments of H. WEBER, as well as of SCHULER, BONER, BUCHHEIM, O. WEBER, arrest of the circulation also gives rise to inflammation or stasis. If, especially in a frog after section of the nerves, the arteries and veins of an extremity be ligated, and then caustic alkalies, ammonia, acetic acid, common salt, carbonate of soda, salt-petre, chloride of calcium, urea, corrosive sublimate, tartar emetic, nitrate of silver, tincture of cantharides, iodide of potassium, etc., be brought in contact with the web, in which the circulation is completely arrested, the blood will stream from out of the arteries into the capillaries and heap up, and even from out of the veins it will flow backward into the capillaries of the irritated region. If the circulation be re-estab-lished the stasis will remain. (If, instead of ammonia, etc., saturated solutions of Epsom salts, sulphate of soda, acetate of zinc, etc., be used, the stasis will disappear after the release of the circulation.) Distilled water, solution of gum, phosphate of soda, alum, tannin, etc., are in free as well as in arrested circulation, without influ-ence.

According to SAMUEL (*Virch. Arch.*, 1868, XLIII., p. 552; 1870, LI., p. 178), inflammation of the ear of the rabbit by cold, heat, or cauterization, offers the same symptoms of acute inflammation as in man. Disturbance of the circulation is the most prominent of all the phenomena. It consists in the "analysis of the blood" (thus SAMUEL terms the accumulation of the colorless blood-corpuscles against the wall of the vessel, etc.) in the veins during the undisturbed blood-flow into them from the arteries. The changes of calibre of the vessels, which, according to COHNHEIM, *et al.*, are essential forces of this "analysis," SAMUEL holds to be contingent. He lays the greatest weight on the CHANGES OF THE VESSEL-WALLS, whereby they lose their smoothness, tone, and contractility. The disturbance of nutrition consists in a changed influence of the internal wall on the blood, in greater permeability of the vessel-wall; finally, in increase in size, whereby the number of channels acces-sible to the blood is increased (new-formation of vessels). Besides, S. lays weight on the whole blood, which is poorer in colorless corpuscles, and on the coagulation of the blood at the focus of inflammation, wherein is a source of emboli. The "blood-analysis" in the veins is more marked than in the arteries, because fluids which may come in contact with the vessel-wall, deprived of their activity in a purely mechanical manner through the strong transudation stream from arterial regions, become, on the other hand, very favorable to it through the current of resorption on the part of the veins.

SAVIOTTI (*Virch. Arch.*, 1870, L., p. 592) describes two series of changes in the circulation in the web of the frog after application of irritants. In one and the most frequent series (by dilute caustic soda, concentrated acetic acid, dilute sulphuric acid, croton oil, ether, solutions of alum, carbonate of soda, saltpetre, soda, etc.) there are dilatation of the arteries, then of the capillaries and veins, and simultaneous accel-eration of the circulation—true active hyperæmia; afterwards, contraction of the arteries and retardation of the circulation—anæmia. Herewith may be connected : anæmia of the capillaries; formation of border zones in the small, less often in the large veins and capillaries, rarely in the arteries, because by arterial contraction the *vis-a-tergo* diminishes, or also in consequence of direct changes of the capillary wall; stasis in the capillaries and small veins, seldom in the large veins, almost never in the arteries. In the second series (especially by ammonia and some of its salts) there appears, immediately after their use, a contraction, first mentioned by the author, of the arteries with retardation of the circulation, which lasts from a few seconds to some minutes Afterwards dilatation of the vessels appears with accelera-tion of the circulation, and then secondary contraction, so-called, of the arteries, with retardation of the circulation. The primary contraction is probably a local phenomenon, and is dependent either upon a direct effect of the irritant upon the arterial wall, or is a local nervous phenomenon. Dilatation is probably also of a local nervous nature, not dependent on a direct action upon the muscles of the vessels. From S.'s experiments it follows that the spasmodic as well as the paralytic theories of inflammatory hyperæmia are founded on fact, but are both incorrect in so far as they are exclusive.

SAVIOTTI saw in GOLTZ's experiment of striking the abdomen of the frog that the arteries of the web contracted, many capillaries became empty, and the cir-culation slow. If after a few seconds the striking was stopped, the circulation soon again became regular. Frequently the arteries passed into a condition of dilatation. Similar to the effects produced in the striking experiment are those of pricking the skin of the abdomen or back, pinching of the finger with the pincers, application of chemical substances upon the body, the electric current. Contractions appear

immediately or in a few seconds after the irritation: usually more intense in the first case than in the second. If contraction takes place at once, the circulation comes to a sudden stand-still. If the appearance of the contraction be comparatively slow, the diameter of the arteries will be shorter, with proportionate diminution of the quantity of blood. The contractions lasts ten to thirty seconds: then the circulation again assumes its previous pace. In veins of medium calibre, only once did S. see a slight contraction. It is doubtful whether it is like that of the arteries or is a consequence of the diminished quantity flowing into them.

S. discusses farther, whether the contractions of the arteries are identical with the rhythmical contraction, so-called, of the arteries which SCHIFF first observed in the rabbit's ear, S. also in frog's web, or whether they depend upon the changes in the heart's action, which appears on irritation of the sensitive nerves (GOLTZ, *et al.*), or whether they are peculiar contractions of a reflex character. From his experiments, S. decides in favor of the latter: the contractions do not appear after section of the sciatic nerve in the corresponding extremity, but in the web of the other limb.

That at the focus of inflammation and in its neighborhood, greater quantities of blood are in circulation, is manifested by the appearance of the part, the pulse-beat, according to MOSENGEIL (*Arch. f. klin. Chir.*, 1871, XIII., p. 70) the fuller and stronger pulse of the corresponding extremity in comparison with that of the other. The change in the pulse is due to a relaxation of the vessel's muscular coat.

The BEHAVIOR OF THE LYMPHATICS of inflamed parts has been little investigated: in part on the dead body, in part experimentally, in part clinically. From clinical observations it has long been known that many substances, especially the poison of dead bodies, and the virus of syphilis, give rise to an inflammation of the lymphatic vessels and glands; special histological investigations of the lymphatics themselves are wanting. A dilatation of the lymphatics, probably with increased function of the same, is recognized in many superficial inflammations of the skin (beneath and about blisters, pock-pustules, etc.), in inflammations of many serous membranes, especially of the pleura with serous, fibrinous, and purulent exudation. More rarely, the dilated lymphatics are filled with fibrinous coagula. Least known is the behavior of the lymphatics in inflamed parenchymata.

LÖSCH (*Virch. Arch.*, XLIV., p. 385) caused traumatic inflammations in the diaphragms and testicles of rabbits and dogs. In the mesentery he observed the lymphatic sheaths in the course of the inflammation collapse more and more, the quantity of the contained lymph diminish, the lymph-stream become slower, and cease entirely. In the testicles inflamed traumatically, the lymphatics were in some cases in great part preserved, not closed, but open and discharging upon the surface of the wound; in other cases, on the contrary, they were, in the immediate neighborhood of the wound, filled with a mass consisting of pus, fat, and detritus. In like manner did most of the remaining cases behave: closure succeeded early, sometimes after twenty-four hours. Never was the closure dependent upon compression by the increased growth of the tissue.

The Author (*Arch. d. Heilk.*, XI., p. 43) found in recent sero fibrinous pleuritis almost constant changes in the lymphatics: most often dilatation of them and filling up with a clear liquid, poor in corpuscles; once filling up of them with a mass like coagulated fibrin. In older cases of pleuritis the endothelia of the lymphatics were mostly enlarged, more cylindrical, not infrequently with double nucleus. In suppurative pleuritis there likewise occur dilatations of the lymphatics, and filling up of them with an albumino-fatty substance. In the neighborhood of common abscesses of the liver there are not infrequently found extreme dilatation of the perivascular lymphatics and a deformity of the hepatic cells, caused by compression.

SCHOTTE (*Arch. f. Anat. u. Physiol.*, 1869, p. 467) observed a tolerably quick and complete absorption of iodide of potassium, etc., by the suppurating pleural cavity. *Vice versa*, after the internal use of these substances, they were again found in the pleural pus.

THE SECOND PRINCIPAL PHENOMENON OF INFLAMMATION IS EXUDATION AND SUPPURATION.

The two products, fluid and cellular exudation (Pus), occur almost always together, but in the most varying proportions.

EXUDATION IS THE MOST IMPORTANT PART OF THE PROCESSES OF INFLAMMATION, and is never absent, although often to be perceived only by the microscope. It is not infrequently the first and, in inflammations of internal organs, the only demonstrable change of the inflammatory process. It occurs alike in vascular and in non-vascular, in solid and soft parts, in membranes and parenchymata.

With respect to their SEAT, exudations are distinguished as free, interstitial, and parenchymatous.

FREE EXUDATION is found upon free surfaces, and within the natura. cavities of the body (external skin, mucous membranes, gland-ducts, acini of the glands, alveoli of the lungs, serous membranes). This exudation is connected more with the processes of secretion.

INSTERTITIAL (or infiltrated) EXUDATION is found between the tissues and parts of tissues, which, if they are firm, it separates; if softer, it destroys (laminated epithelium, connective tissue of the most various parts, brain, etc.).

PARENCHYMATOUS EXUDATION, which has its analogue in common nutrition, is seated within the tissues themselves, especially in epithelial and glandular cells of every kind, in connective tissue and bone-corpuscles. The cells become larger, their contents more abundant, and for the most part more clouded by molecules of albumen than in the normal state: albuminous infiltration.

In many cases two and even all three exudations are found at the same time in the same organ.

While the two latter exudations mostly remain a longer time, free exudation is either immediately or after a shorter time passed to the exterior (intestinal canal, urinary passages, etc.); or it penetrates still deeper into the organs (e.g., from out of the smallest bronchi into the alveoli of the lungs)—displacement and retention of the exudation.

The QUANTITY OF EXUDATION varies extremely: according to the intensity of the causes of the inflammation, the character of the exudation, its seat, and the kind of tissue affected. It varies from a minimum to many pounds. The most abundant are the free exudations of serous membranes and many mucous membranes.

With respect to QUALITY, EXUDATIONS are SEROUS, MUCOUS, FIBRINOUS, and MIXED. In each of these exudations there is a slight admixture of cells analogous to colorless blood-corpuscles. If their quantity be increased, there result PURULENT EXUDATION, or the mixed forms of this: the SERO-PURULENT, the MUCO-PURULENT, the CROUPOUS, and the DIPHTHERITIC. If the exudation contains red globules in greater quantity, it is called HÆMOR-RHAGIC. All these exudations show transitions among themselves.

The CHEMICAL CHARACTER of the exudations is on the whole still obscure: because they are almost never examined in the fresh state and are rarely pure, because of the existing imperfect knowledge of albuminous bodies, etc.

SEROUS EXUDATIONS are not essentially different from transudations. They are mostly clouded by colorless blood-corpuscles, more rarely by small portions of fibrin, by cells separated from the organs affected, and by oil-globules. In other respects serum has all the peculiarities of blood-serum, except that it has somewhat less albumen and more water. Serous exudations upon free surfaces are called FLUX (SEROUS CATARRH); into serous cavities, INFLAMMATORY DROPSY; into tissues, INFLAMMATORY ŒDEMA; under the

epidermis and uppermost layers of the pavement epithelium of the mucous membranes, SEROUS VESICLES, etc. A serous exudation containing more albumen is called ALBUMINOUS. It is found in many inflammations of the kidneys, where albuminous urine is excreted (albuminuria), of the intestinal canal (dysentery), etc. To this class belongs also parenchymatous exudation (*vide supra*). Between serous and albuminous exudations there are numerous transitions.

An essential distinction was formerly held to exist between inflammatory exudations and dropsical effusions. Since, however, A. SCHMIDT (p. 155) has shown that all transudations are coagulable, and that the red blood-corpuscles (because they could be replaced by a solution of hæmatoglobulin), induce coagulation chemically (not in their character as living cells), this distinction comes to nothing.

DONDERS (*Nederl. lanc.*, Nov., 1849) found the clear watery liquid, which is discharged in the first stage of nasal catarrh, with a strongly alkaline reaction ; in its drying up there are formed abundant crystals of sal-ammoniac, less of common salt.

Many serous exudations are probably founded on affections of the nerves. Thus, *e.g.*, primary and metastatic serous, or polymorphous parotitis (mumps). This accords, perhaps, with the teaching of the known physiological experiment. If the excretory duct of the submaxillary salivary gland be ligated, and the nerve arising from the *chorda tympani* irritated, the gland will become filled with saliva. After the secretion is exhausted, there appears a form of œdema of the gland, whereby it becomes three to six times larger than the gland of the other side, and the lobules separated by wide intervening spaces ; in these, as in the vicinity of the glands, there is found an abundant serous liquid.

Concerning the formation of vesicles in the skin of man, consult VOIGT, *Arch. d. Heilk.*, 1869, X., p. 240 ; concerning that in the skin of the frog, BIESIADECKI, *Unters.*, 1872, p. 60.

MUCOUS EXUDATION is sometimes not to be distinguished from normal mucus, sometimes it is thicker, mostly, however, thinner than the latter. It occurs oftenest on mucous membranes, and forms MUCOUS CATARRH. These exudations have their origin in the production in increased quantities of liquid mucus by the epithelium of the mucous membrane and mucous glands, and in the mixing of this with the increased flow from out of the vessels, or migrated colorless blood-corpuscles.

Noteworthy CHANGES in the three above-mentioned exudations seldom occur, especially because soon after formation they are removed from the body. Otherwise they manifest not infrequently a sort of inspissation, which in mucous exudation may, in turn, be followed by liquefaction.

FIBRINOUS EXUDATION consists of fibrin, which the hyperæmic vessels yield in liquid form, but immediately after its exit from the vessels it coagulates into fibres, and within the spaces between these serum is confined. Besides the fibrin, the serum is found in varying proportion : sometimes so little of it, that it is only confined within the intermediate spaces of the fibrin : TRUE FIBRINOUS EXUDATION ; sometimes in greater quantity within the cavity of the serous sac : SERO-FIBRINOUS EXUDATION. The serum then is clear or cloudy. There are almost always mixed with the exudation pus-corpuscles, *i.e.*, migrated white blood-corpuscles, in varying quantity ; abundant admixture of these constitutes the FIBRINO-PURULENT EXUDATION. All these exudations occur purest on the surface of serous membranes.

According to A. SCHMIDT. coagulation of inflammatory exudations upon free surfaces, as well as within parenchymata, is dependent partly upon the admixture of blood-corpuscles, partly upon the distention of the bloodvessels with blood-corpuscles. Thereby the pressure upon the vessel-walls is considerably increased, so that a transudation takes place, not as in dropsy through healthy vessels, but through those that are diseased, and acts like a foreign substance.

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FLEMMING (*Virch. Arch.*, 1872, LVI., p. 146) holds that the fine fibrinous net-work in artificial inflammation occurring in the subcutaneous connective tissue of dogs and rabbits does not have its origin in the blood, but is a secondary product of the inflammatory state.

The fibrinous exudation of serous membranes is at first a very thin, hardly recognizable, variously thick (to many lines), sometimes homogeneous, sometimes in places or throughout netted or flaky, moist and translucent layer of gray or yellowish-white color, and adheres quite firmly to the subjacent tissue. The section-surface is likewise colored, moist in varying degree, seldom entirely uniform, and likewise for the most part reticulated.

MICROSCOPICALLY, fresh fibrinous exudation appears rarely as an uniformly thin, bright substance, from which numerous irregular tufts stand out ; it forms mostly a net-work of fine fibres of varying thickness and size, rounded, with the intervening spaces filled with serum. The endothelia of serous membranes are preserved under the exudation, sometimes normal, more rarely clouded, or having many nuclei. The lymphatics of the serous membranes are for the most part widely dilated, filled with clear liquid, also in rare cases with fibrin. The older and thicker exudation of fibrin consists of the same fibrin-fibres, in whose larger spaces serum is found partly free, partly confined in a fine fibrous net-work. With the serum are admixed mostly common or swollen pus-corpuscles. The endothelium of serous membranes reacts sometimes as in fresh exudations, sometimes it is increased. The lymphatics are usually still farther dilated. The serous membrane itself is normal in pure cases of fibrinous exudation.

Consult the Author (*Arch. d. Heilk.*, 1870, XI., p. 43), as well as the different statements of VIRCHOW, BUHL (l. c.), RINDFLEISCH (*Lehrb.*, 1871, p. 226). According to RANVIER (*Nouv. dict.*, 1870, XIII., p. 675), endothelia are again found in the midst of the fibrinous layers of the serous membranes : they have very odd forms, and often contain a very great number of nuclei, like giant-cells.

IN OTHER ORGANS pure fibrinous exudation seldom occurs. Especially do the so-called fibrinous exudations upon mucous membranes, perhaps also those in the lungs and kidneys, have a character similar in gross to coagulated fibrin, but under microscopic investigation, etc., are for the most part altogether different (see Croupous exudation). Mixtures of fibrin, on the other hand, are not infrequently found, especially in serous exudations : also upon serous membranes in inflammatory exudations of the epithelium and of the corium of the skin and of mucous membranes, in many intense inflammations of the sub-mucous tissue, of the stomach, intestines, etc.

The METAMORPHOSES of fibrinous exudation are : desiccation, connective-tissue-like transformation, fatty degeneration, and calcification. These never affect the fibrin alone, but always also the serum and the cells in it.

DRYING, CORNIFICATION, shrivelling up of the fibrin takes place only in small quantities of it. It becomes gradually harder and drier, can no longer be split into fine fibrillæ, but only into flake-like fragments ; acetic acid gradually loses its effect upon it. The fibrin is changed into a HOMOGENEOUS or COARSE-FIBRED, CONNECTIVE TISSUE-LIKE mass, which swells up in acetic acid, but neither cell-nuclei (except perhaps those of the included colorless blood-corpuscles) nor connective tissue corpuscles appear : FIBRINOUS TISSUE. The fibrin swells up from absorption of serum, becomes softer, translucent : ŒDEMA of the fibrin. In the fibrin there appear numerous very small OIL-GLOBULES. In less degree this takes place mostly very soon after the excretion of the fibrin, and then is only to be seen by microscopic examination. In higher degree it introduces resorption of the fibrin : the exudation becomes yellowish and grayish, brittle and greasy. Fatty metamorphosis for the most part

affects only the cells included within the fibrin. The fibrin CALCIFIES, becoming a fixed, continuous stone-like mass, or a kind of mortar, the exudation thereby becomes less, and assumes a whitish or yellowish color.

The mode of RESORPTION of fibrinous exudations is in detail still little known. The purely fibrinous portion of such exudations appears first to pass through a sort of liquefaction. The serum is simply resorbed as the resorbing vessels are again accessible, or are newly formed.

In cases of pleuritic exudations the opportunity is sometimes had of convincing one's self of their long duration, and of the trifling changes of the fibrinous portion of the exudations. In four such cases, which afforded a topsies, one to four years after the beginning of the exudation, I saw the fibrinous masses attached to the thickened costal pleura, still thick and little changed microscopically. The microscope showed only fatty metamorphosis of the cells within the fibrin, which itself had not suffered any essential change.

A so-called ORGANIZATION of the fibrin, *i.e.*, a transformation of it into vascular connective tissue does not occur. Formerly fibrinous and "plastic" exudations were held to be identical, from which were developed psendo-membranes, hypertrophy of the connective tissue of organs, cicatricial tissue, etc. Where fibrinous exudation and new-formed vascular connective tissue happen together, the latter had its origin from the original tissues and grew into the latter.

PURULENT EXUDATION occurs either in a pure state, or is mixed in varying proportions with the other exudations. Pus is its essential ingredient.

Pus in a pure and fresh state is a creamy, yellowish liquid without odor, or with a somewhat sweetish smell, and with an alkaline reaction. It consists of pus-serum and pus-corpuscles.

Pus-SERUM is a clear, pale or light-yellow liquid with alkaline reaction. It is coagulated by boiling. Its essential ingredients are water, albumen (1–4 per cent.), fibrinoplastic substance, salts like those of blood-serum and extractive matters. In pus, which has suffered change, are found casein, mucin, pyin, etc. Sometimes serum is almost entirely absent in fresh pus.

Pus-CORPUSCLES (pus-cells) resemble the colorless blood-corpuscles.

Pus-corpuscles are round, granular, about 0.01 mm. in diameter, not infrequently smaller or larger, contractile and movable. Their so-called membrane is smooth or uniformly mammilated. Their contents are uniformly granular, and possess little or no transparency. After the addition of various substances, there appears a single, double or triple, or even a manifold nucleus, commonly without nucleolus; the nuclei vary according to their number in size, are round or oval, sharply defined, bright, sometimes showing a central depression. Under the action of common or distilled water, or very thin liquids (*e.g.*, urine), very dilute acids, etc., pus-corpuscles enlarge, their membranes becomes smooth, their contents in consequence of the absorption of water transparent, their nuclei prominent, many at last burst; in many the nucleus also swells up. By acetic acid, and dilute mineral acids the membrane and contents become so transparent that only the nuclei remain visible; the latter have a sharper contour and are smaller. By solutions of neutral alkaline salts pus-corpuscles are made to shrivel together and lose their sharp contour. By caustic alkalies, bile, solutions of glyco- and tauro-cholate of soda, they are destroyed.

According to HUIZINGA (*Med. Centr.*, 1868, No. 4), pus-cells (from a frog's eye which had been inflamed by cauterization by nitrate of silver) instantly become globular by carbonic acid and ammonia, and lose all contractility.

Besides the common pus-corpuscles, there are sometimes also found those which are twice as large, and sometimes contain only one or few, sometimes very many nuclei. It is doubtful whether they represent a simple hypertrophy (BIZZOZERO), or whether they owe their origin to a coalition of two colorless blood-corpuscles (AXEL KEY).

Not infrequently pus stinks, without being in a high degree corrupt, from the sulphuretted hydrogen, which is formed out of the protein compounds of pus. Bone-pus sometimes smells because of phosphuretted hydrogen. In localities on

the skin supplied with numerous sebaceous glands, the smell of pus reminds one of butyric acid. Pus commonly stinks worst, when it has had its origin near the intestinal canal and there has stagnated a long time, as in abscesses of the abdominal muscles, circumscribed suppurative peritonitis: due in each case to a diffusion of intestinal gases.

Concerning the chemical composition of pus, consult MIESCHER (*Med.-chem. Unters.*, 1871, 4. H., p. 441), and HOPPE-SEYLER (*Ib.*, p. 486). According to MATHIEU (*Gaz. hebd.*, 1871, 14. July and 1872, No. 21), O. is entirely or almost entirely wanting in pus, while H, N. and CO_2 are present. H also is rarely found. N is present in small quantity, CO_2 always in large quantity (27–109 vol. $\%$).

SPECIFIC PUS, so-called (syphilitic pus, small-pox pus, pus of glanders), is not distinguished histologically and chemically from common pus (*vide* Pyæmia).

Besides pus-corpuscles, pus contains almost invariably free nuclei, some red blood-corpuscles, sometimes also ACCIDENTAL ADMIXTURES, as epithelium, connective tissue remains, crystals of the triple phosphates, infusoria, etc.

Sometimes pus is not yellow-colored, but has a reddish, bluish, or green color.

The causes of the many PECULIAR COLORS OF PUS are known only in part. A yellowish-red or reddish coloring depends almost always upon the blood, rarely upon crystals of hæmatoidin. The BLUE (and the rarer GREEN) pus depends, according to MÉRY, KREMBS, LÜCKE, and others on a vibrio. This is probably brought with the dressings into contact with suppurating or moist wounds, and by the warmth of the body, moisture and albuminous nutriment, they increase so greatly that the dressings are colored blue by it. Besides, pus is never blue, but always the dressings saturated with pus-serum, often also the epidermis. CHALVET has observed, and LÜCKE has experimentally demonstrated, that wounds in the neighborhood may become infected from those sick with wounds which secrete blue pus. The blue color can be separated in crystalline form, pyo cyanin (FORDOS and LÜCKE). As pyo-cyanin appears sometimes blue, sometimes green, so the color changes also on the compresses, sometimes in the same individual, and in the transporting substances green may come from the blue, and *vice versa* A thick creamy pus and excessive secretion of it offer an unfavorable soil for the development of vibrios. The progress of disease as such has no influence upon the development of vibrios, and their presence has as little upon the process of healing (LÜCKE. *Arch. f. klin. Chir.*, III., p. 135).—Many cases of blue pus depend upon the excretion of vivianite (H. SCHIFF).

The RELATION OF PUS TO THE TISSUES varies. Either pus is found on the SURFACE of the skin, mucous membranes, inclusive of the gland-ducts (blenorrhœa, pyorrhœa), serous membranes (empyema): EPITHELIAL, SECRETORY, or SUPERFICIAL SUPPURATION; or it lies in the INTERIOR of membranous or parenchymatous organs: PARENCHYMATOUS or DEEP SUPPURATION.

If the PUS IS ON THE SURFACE of organs, the corresponding membranes, etc.; beneath, are, to the naked eye, either normal, without loss of substance, etc., or they show small and the least superficial losses of substance—affecting the epithelium—often recognizable only by attentive observation, or with the lens: EROSIONS; or they form an ULCER, *i.e.*, a deeper loss of substance, not only affecting the epithelium, but even extending into the tissue of the affected membrane, a solution of continuity, which heals sometimes quickly, sometimes from local or general causes more slowly, or, indeed, not at all, and is the source of a continuous formation of pus. Individually, ulcers are of very different character: first, with respect to their form, (round, etc., superficial or deep); then with respect to the character of the base and its secretion (serum, pus, ichor, etc.), then with respect to that of the edges (soft, hard, callous, undermined, etc.), and of the neighboring tissues (normal, inflamed, pigmented, etc.) If the ulcer is sinuous it forms,

for example, a communication between the skin externally, or a mucous membrane on the one hand, and a deep-lying organ on the other hand, and is called a FISTULA in the broader sense, or FISTULOUS ULCER. A fistula, in the narrower sense, is a communication between the skin or mucous membrane and a gland or gland-duct, and gives passage to a part of the glandular secretion.

If the PUS lies IN THE INTERIOR of membranous or parenchymatous organs, it assumes either the form of an ABSCESS (*abscessus, apostema*), *i.e.*, it is deposited into a sharply defined, new-formed cavities of varying size, which are more rarely located in epithelia (EPITHELIAL ABSCESS), oftener in other kinds of tissue (COMMON ABSCESSES). In the locality of the abscess the affected parts of the parenchyma (fibres of all kinds, glandular cells, bone-substance, etc.) for the most part disappear, to a small extent are pushed to one side. Or the pus takes the form of an INFILTRATION, of a diffuse abscess, *i.e.*, the ingredients of pus lie between the connective elements (purulent infiltration, suppurative inflammation, with a greater proportion of serum, purulent œdema). The connective elements are thereby at first only pressed together. But if the pus is not soon removed they soften and disappear in different ways in different tissues: SUPPURATIVE LIQUEFACTION. Especially distinct is this in transversely striated muscles, in the liver, brain. Purulent infiltration is the first step of abscess.

In the tissue around the purulent infiltration and most fresh abscesses there is found a collateral hyperæmia and œdema, which latter sometimes consists in a tenser filling of the lymphatics. The tissues around older abscesses, as well as all chronic ulcers, exhibits an induration of tissue: INFLAMMATORY INDURATION. This happens when the vessels are hyperæmic, and the connective tissue corpuscles increase or are filled with albuminous masses. The surrounding tissues can finally, in the whole circuit or only here and there, pass into suppuration: the latter then results in the OPENING or PERFORATION OF THE ABSCESS.

METASTASTIC ABSCESSES are distinguished from common abscesses, especially by their origin. The former are found especially in the lungs, liver, spleen, kidneys. They occur usually in greater number, are mostly at the periphery, and oftener have a wedge-shaped than a round form (see p. 206).

ABSCESS from CONGESTION, or wandering abscess, arises when a common abscess spreads out in one direction on account of the too great resistance of the surrounding structures, where the surrounding parts are looser, more easily separated from one another, and brought into a state of inflammation: *e.g.*, under fasciæ, periosteum. SOLTMANN (*Med. Ctrlbl.*, 1872, No. 42) has more accurately followed the first steps of congestive abscess on the basis of anatomical experiment. Consult also KÖNIG (*Arch. d. Heilk.*, 1870, XI., p. 221); BILLROTH (*Ueb. d. Verbreitungswege d. entzündl. Proc.* In *Volkm. Samml. klin. Vortr.*, 1870, No. 4), and HENKE (*Unters. d. Ausbreitung des Bindegewebes mittelst künstlicher Infiltration*, 1872).

Pus sometimes occurs pure, sometimes mixed with serous liquid (sero-purulent exudation), with mucus (catarrh of mucous membranes, blennorrhœa, pyorrhœa), with fibrinous exudation (purulo-fibrinous exudation), with blood, etc.

The origin of pus is accurately known for certain localities by experimental investigations. PUS-SERUM IS THE EXUDED LIQUOR OF THE BLOOD: SEROUS EXUDATION. THE PUS-CORPUSCLES ARE ALL, OR BY FAR THE GREATEST PORTION OF THEM, in vascular as well as in non-vascular tissues, MIGRATED WHITE BLOOD-CORPUSCLES; A SMALL PORTION HAVE PERHAPS A DIFFERENT ORIGIN. Until now the following modes of origin have been in part observed

on the living animal, in part inferred as a matter of probability, from examination of dead tissues: division of pre-existing cell-forms (epithelium, connective tissue, corneal and muscle corpuscles), division of wandering cells, and of pus-corpuscles themselves; endogenous cell-formation, by the common mode with division of the nucleus (in cartilage-cells) as well as especially by the free mode, *i.e.*, without division of the nucleus (particularly in epithelium); metamorphosis of fixed spindle-shaped or radiate connective tissue and analogous corpuscles into movable or wandering cells.

Observations upon dead, fresh or hardened preparations, with respect to the question of the origin of pus, become of value only with more fixed regard to experimento-pathological results. With respect to the migration of colorless corpuscles from out of the veins and capillaries, those preparations speak in favor of it, which in the immediate vicinity of those vessels show bordering rows of pus-corpuscles, as in many acute inflammations of the skin (variola), in suppurative meningitis; also those in which those vessels are distended with white blood-corpuscles, like those in many granulations. With respect to the other mode of origin, there are results which have been reached in acute catarrhs of the mucous membranes and in recent inflammations of serous membranes, and which indicate that pus-corpuscles have their origin within, or out of epi- or endothelium.

REMAK (*Virch. Arch.*, XX., p. 198) first found an endogenous origin of pus-corpuscles in the epithelium of the urinary bladder. BUHL (Ib., XVI., p. 168; XXI., p. 480) saw the same in the epithelium of the lungs and bile-ducts. RINDFLEISCH (Ib., XXI., p. 486) places the origin of pus-corpuscles in artificial catarrh in animals and in man in the epithelium or sub-epithelial connective tissue. BÖTTCHER (Ib., XXXVIII., p. 428) observed endogenous formation of pus-corpuscles in the gums. EBERTH (Ib., XXI., p. 106) saw the same. But all these results can be explained also in other ways. The epithelial suppuration discovered by EIMER (*Virch. Arch.*, XXXVIII., p. 428) in the intestinal canal, was later by himself pronounced to be a development of psorosperms. According to VOLKMANN and STEUDENER (*Med. Centr.*, 1868, No. 17, and *Arch. f. micr. Anat.*, IV., p. 188), the appearance of an endogenous cell-formation in cancers and during suppuration may also have its origin in that smaller cells (in suppuration. *e.g.*, the migrated colorless blood-corpuscles) are pressed into larger ones, and are completely inclosed within them. HELLER (*Erlang. Sitzsber.*, May, 1872) also has shown that in intense catarrh of mucous membranes there is an increase of the physiological production of epithelial elements, and that a part of these formations, without farther development, may be mixed with the secretion being discharged. These also may exist as transition forms between epithelium and pus-corpuscles. See also BIZZOZERO's observations on the anterior chamber of the eye (l. c., p. 325).

The white blood-corpuscles in many localities besides passing through the walls of the veins and capillaries, pass through a second membrane essentially different in structure; in the trachea and bronchi in catarrhal and croupous inflammations the, at least in the former locality, thick basement membrane; in the kidneys, the wall of the urinary tubules; in the cornea, in many forms of pannus the anterior layer.

Observations of RINDFLEISCH, IWANOFF, A. KEY.

The CAUSES OF SUPPURATION are those of inflammation chiefly, as soon as these reach a high grade. In external parts the causes are especially wounds, in which are foreign bodies of more or less irritating character. Suppuration occurs very easily in some internal organs (mucous membranes, serous membranes, lungs), more rarely in others (muscles, bones), or very rarely (thyroid gland).

METAMORPHOSES OF PUS appear, if it is not removed from the body, naturally or artificially, immediately after its formation. They affect the corpuscles as well as the serum. They are of importance with respect to the future of the pus itself, of the affected tissues, and sometimes of the whole organism.

RESORPTION of pus, and of the serum directly, of the corpuscles perhaps by migration again into the lymphatics, but mostly after previous fatty metamorphosis, occurs in a greater or less degree as well in pus of the natural cavities of the body as in that infiltrated, and in abscesses.

EVACUATION of pus takes place upon the external surface, upon mucous membranes, through normal orifices, out of internal organs after previous communication with those parts.

INSPISSATION, or CHEESY METAMORPHOSIS of pus, by resorption of the serum and simple atrophy, sometimes also at the same time by fatty metamorphosis, or partly by calcification of the pus-corpuscles, is found especially in deposits of pus in natural cavities communicating or not with the surface of the body, and in abscesses. Thereby pus becomes changed into a thick, more or less dry, even cheesy, grayish-yellow mass, which bears the closest similarity to yellow tubercle. Therefore this transformation is also called TUBERCULIZATION of pus. Many tubercles, so-called (e.g. of the lungs, lymphatic glands, bones, etc.), are nothing more than deposits of pus thus transformed. The CAUSES of this change lie partly in local, partly in general conditions. The former are found especially in the fine bronchi, and in osseous tissue; the latter in man with the so-called tuberculous habit. In rabbits cheesy transformation of pus is a regular process.

Cheesy foci are, according to BILLROTH, sometimes present from the beginning. They arise in an accumulation of new-formed cells without liquid inter-cellular substance, the latter in consequence of less vascularization. B. calls the process "non-vascular or dry necrosis." Something similar is seen in the rabbit after the passage subcutaneously of a seton; after a few days there is found around the seton, not common pus, but a yellow, cheesy mass.

CALCIFICATION of pus occurs rarely in large deposits of pus, or only in a part of them, and is the origin of concretions varying in hardness to that of a stone.

MUCOUS METAMORPHOSIS of pus, especially of pus-corpuscles, occurs in many large and small pus-cavities, in pus of the alveoli of the lungs (in pneumonia), etc.

ICHOROUS TRANSFORMATION, or putrefaction of pus, consists in its change into a sometimes pale, sometimes (by hæmorrhage) brownish, thin liquid, ICHOR, which has a bad smell, and corrodes normal and pathological structures. Under the microscope pus-corpuscles are seen in very small quantity, are even almost wanting, their granular condition is gone, their nuclei are distinct. Besides, there are found flattened, fatty, and simply atrophic pus-corpuscles.

CROUPOUS EXUDATION, on account of its similarity with fibrinous exudation, is in many ways confounded with it, but from its nature and origin is entirely distinct from it.

Croupous exudation is found almost only upon superficial organs, which are covered by a true, mostly laminated epithelium; upon mucous membranes (oftenest on the tonsils, gums, throat, air-passages, more rarely in other parts), in a modified way also under the horny layer of the skin. It sometimes occurs pure, sometimes in transitions into mucous or purulent exudation. On the mucous membranes mentioned it forms either a sub-

stance extended over larger surfaces, and, with respect to its form, flat, tubular, or cylindrical, grayish-white, homogeneous or reticulated, little transparent, elastic and similar to freshly coagulated fibrin; which substance at first adheres quite firmly to the subjacent layer: CROUPOUS MEMBRANE; or, larger or smaller, isolated, similarly constituted spots: DEPOSITS. After a little time the exudation (membrane as well as deposit) is colored somewhat darker (more yellowish or dirty), and becomes less elastic and loses its connection with the subjacent layer. The latter, the affected mucous membrane, etc., is at first intensely hyperæmic and uniformly swollen. After spontaneous separation of the croup-membrane the hyperæmia disappears; if in the meanwhile death does not supervene, the mucous membrane is completely restored to its normal state.

MICROSCOPIC EXAMINATION of the croup-membrane reveals a light, homogeneous, bright, 0.02–0.002 mm. thick, net-work, the rounded spaces of which contain mostly serum, or pus-corpuscles, or free nuclei, sometimes single epithelial cells, in many cases also red blood-corpuscles. The upper (free) layer of the net-work is a laminated epithelium, at first covered by the uppermost layer of cells; later, this layer disappears, so that the net-work is naked or covered by various forms of fungus. The lower surface of the network (toward the mucous or cutaneous tissues, etc.) limits the lowest layer of the (unchanged) epithelium, or lies immediately upon the surface of the hyperæmic cellular infiltrated or non-infiltrated mucous membrane, etc. The net-work itself shows a remarkably great resistance to heat and all chemical reagents.

The net-work of croup-membrane occupies the PLACE of the EPITHELIUM, and has its origin in a peculiar metamorphosis of that epithelium. While the epithelium in common epithelial suppuration is quickly ruined by softening, etc., here it is transformed into peculiarly broken masses, the remains of which are not filled by cells or liquid like the other resistant net-work which resembles coagulated fibrin.

CROUPOUS METAMORPHOSIS, so-called, of epithelium begins with a general enlargement of the cells, which depends upon an increase of the protoplasm. Therein arise many points, up to 0.01 mm. in size, for the most part sharply defined from the beginning, round or oval, at first in the periphery, later at the centre of the cells. Between these the cell-substance becomes darker, brighter, and presents a porous or indented appearance, dependent on the number and arrangement of those points: at the same time it becomes strikingly resistant. Besides, during the gradual disappearance of the nucleus similar new points arise, whereby the whole cell assumes an appearance still more porous. The points in the beginning are still surrounded, here and there, by thicker or thinner protoplasmic layers, until the latter entirely disappear, and the cells become pierced by a great number of pores and are toothed at the periphery. These projections are fused with the neighboring cells, but can be again isolated by artificial means. The round cells often appear empty; oftener, however, they contain a nucleus or a pus-corpuscle whose origin is still a matter in question: probably the latter are immigrated colorless blood-corpuscles. Besides epithelia thus changed, are always found those which contain either only one pus-corpuscle, or many such in one round or oval cavity—six and more.

The microscopic processes here just described are best demonstrated by placing fresh membranes into MÜLLER's fluid, whereby they finally break up into the original porous masses, of which each corresponds to an epithelial cell. Information is sometimes furnished also by sufficiently fine sections which at the same time include the border of the croupous deposit and the normal surrounding tissue.

The above view of the author has been met by many doubts. NASSILOFF (*Virch. Arch.*, L., p. 550) explains the peculiar changes of form of the epithelium by the fact, that the cells have become contractile in the same manner as this happens in corneal epithelium from irritation (RECKLINGHAUSEN, HOFFMANN, STRICKER). In another place N. declares the fibres of the net-work to be fibrin.

According to OERTEL (*D. A. f. kl. Med.*, 1871, VIII., p. 242), the peculiar cells of the croupous membrane have their origin through coagulation of the hyaline movable protoplasm. The latter has its origin in the fluid contents of the epithelial cells; the membrane is not concerned in it; the nucleus often shows processes of division. On another point, O. believes that most of the peculiarly formed epithelial remains have their origin in vegetation-processes of fungi, which have drawn from them a part of their nourishment.

Consult further the adverse views of BOLDYREW (*Arch f. Anat., Phys., u. s. w.*, 1872, p. 75) and STEUDENER (*Virch. Arch.*, 1872, LIV., p. 500). Both regard the net-work analogous to the fibrinous net-work of inflamed serous membranes.(?)

CROUPOUS-DIPHTHERITIC EXUDATION occurs in the same localities, as pure croupous exudation, oftenest on the soft palate and tonsils. The surface of the affected mucous membrane shows sometimes the same connected MEMBRANE, as in croupous exudation; sometimes only the DEPOSITS are found. THE TISSUE OF THE MUCOUS MEMBRANE ITSELF, however, not infrequently also the sub-mucous and even still deeper tissues (muscle-fibres), are from the beginning much MORE INTENSELY HYPERÆMIC and MORE SWOLLEN. After a few days the hyperæmia disappears, the parts are now so closely occupied by pus-corpuscles and free nuclei, here and there also by extravasated blood, that they appear thickened, bloodless and uniformly gray or grayish-yellow or brownish-red; and in the HIGHER grades of the disorder a return to the normal state never happens, but instead a gangrenous throwing off of the infiltrated parts.

Between the croupous and croupous-diphtheritic exudations there is every possible transition, whilst sometimes the epithelial change, sometimes the infiltration of mucous membrane, preponderates. The severer forms of the latter form the PURE DIPHTHERITIC EXUDATION of authors.

DIPHTHERITIC EXUDATION is, according to the old view, a common fibrinous exudation, which is not deposited, or only in part, upon the free surface of the inflamed part, but altogether or in great part within its tissue, and on this account is followed by a compression of the vessels and gangrenous death of the tissue. According to VIRCHOW (*Hdb. d. Path.*, I., p. 292; *Deutsche Klin.*, 1864, No. 4), there is no exudation, but the tissue-elements, especially the cells, are found to be quickly filled with a cloudy substance and to be destroyed by fatty metamorphosis: according to this the principal thing is necrobiosis.

According to BUHL (l. c.), diphtheritic exudation (diphtheritis, diphtheria, acute necrosis, etc.) has its origin in a " fibrin-like connective tissue growth " of such high grade, upon free surfaces as well as in parenchymata, that compression of the new-formed and old vessels, anæmia, and finally destruction of the new-formed and old tissue, result. Through abundant appearance of molecules into the cells and fluid parenchyma it becomes cloudy and yellow, dry and brittle. If the crusted mass be taken off, there will be left a loss of substance or an ulcer, which affects only the pseudo-membrane, or at the same time also the subjacent membrane. If the crust be confined to the pseudo-membrane only, there will go on under it an active regeneration of the epithelium, which results in a removal of the crust. If encrusted pseudo-membrane remains in connection with the part affected, it becomes cheesy and then represents a form of yellow tubercle: this is resorbed, or it crumbles off and leaves a loss of substance. If the crust also reaches into the skin lying under the pseudo-membrane, the skin degenerates or there results, after falling off of the crust, a loss of substance, which may be regenerated out of the connective tissue. In a later work BUHL regards " diphtheritic infiltration " as consisting of cells analogous to the colorless blood-corpuscles, but especially of free nuclei. Like all others, he places the greatest stress upon the number of nuclei and upon the resulting anæmia and necrosis. He shows, besides, the analogy of the diphtheritic infiltration with the infiltrations of other infectious diseases, *e.g.*, of indurated chancre, tuber-

culous infiltration, epidemic cerebro-spinal meningitis, etc. He regards diphtheritis as a general disease, and proposes therefor the name '' acute tissue-necrosis;'' he proposes this as opposed to inflammatory, typhous, scarlatinous, tuberculous, etc., tissue-necrosis. Croup and diphtheritis B. regards as widely distinct.

OERTEL (l. c.) found in diphtheritis the often great, nuclear infiltration, not only in the diphtheritic mucous membrane, but in almost all organs, as, e.g., in the lungs, in the connective tissue of the muscles, in the kidneys, stomach, vessel-walls, nerve-sheaths, cerebral and spinal meninges, even in the gray substance of the spinal cord.

The relation of the croupous and of the croupous-diphtheritic or of the pure diphtheritic exudation to one another probably varies in different localities and different times. It possesses the greatest interest in diphtheritis of the throat and laryngeal croup. In the lighter forms of pharyngeal diphtheritis occurring here (in Leipsic) there is found a croup-membrane of the affected mucous membrane, after the falling off of which the hyperæmic mucous membrane itself is uninjured, and the epithelium is quickly regenerated. In severer cases either the same croup-membrane of the palate (tonsils, palate-arches, uvula, etc.) is present, but the danger depends upon its extension into the larynx. Or, on the parts mentioned of the palate there is found beneath the croup-membrane a dense cellular and nuclear infiltration, which in rare cases becomes dangerous from gangrene.

In the greater number of fatal cases of laryngeal croup, diphtheritic exudation is found on the soft palate; croupous exudation in the larynx, trachea and large bronchi; catarrhal, i.e., muco-purulent exudation in the fine bronchi, especially of the lower lobes.

A combination of epithelial suppuration with diphtheritis, I found, oftenest in the œsophagus, in two different forms: either in parts of its superficial mucous membrane pus is found in most of the epithelium, while the remainder shows the croupy metamorphosis; or pus-formation is shown in sharply circumscribed portions of the epithelium, while other in sharply circumscribed portions show croupous metamorphosis (l c. p. 457).

The RELATIONS of croupous and of diphtheritic exudations TO THE WHOLE ORGANISM vary notwithstanding numerous histological analogies. Pure croupous exudation has an especial local action which in certain localities (larynx) is often fatal in children from purely mechanical causes. The lymphatic glands belonging to the affected mucous membrane are only little swollen. Pure diphtheritic exudation is associated with a severe, for the most part febrile general disturbance, related in the same manner as are the eruption on the skin and the constitutional symptoms in acute exanthemata, whilst others regard the general disturbance as consequences of the local pharyngeal diphtheritis. The lymphatic glands concerned swell in a short time and usually to a great degree. In severer cases of pharyngeal diphtheritis there are not infrequently found albuminuria, and hæmorrhages in various parts of the body; and therewith fever of varying intensity, etc. Between these two forms there occur manifold transitions.

The numerous clinical, histological, and experimental works which for years past have made up our literature, have upon all these practically so important questions (and treatment) furnished very little information. Practitioners are in part unable to distinguish many common inflammations of the throat and pharyngeal diphtheritis. Also many histological works are on similar grounds useless. Experimenters have not taken the trouble to investigate with accuracy, whether the diseases called forth by them in animals agree with those in man. Add to this, that in the same place at different times, still more in different places, there appear very different cases especially of pharyngeal diphtheritis. Croupous metamorphosis probably occurs only in the above described croupous deposits and croup-membrane. Many other croupous exudations, so-called, as of the intestinal canal, urinary bladder, etc.,

are of a purely fibrinous nature. Still other croupous exudations, as of the intestine in dysentery, of the uterine mucous membrane in many croupous and diphtheritic forms of endometritis of the puerperal state are dependent upon compact cell and granular deposits into the tissue of the mucous membrane itself. The origin of croupous exudations of the bronchi in chronic croupous or fibrinous bronchitis, in croupous pneumonia, etc., is not yet sufficiently well established.

The word "diphtheritis" or "diphtheria," first introduced by BRETONNEAU, is used in very different senses: sometimes etymologically (membranous), histologically (fibrino-purulo-hæmorrhagic infiltration); sometimes symptomatically (gray-yellowish deposits upon or within the mucous membrane); sometimes clinically; sometimes epidemiologically; sometimes, finally, in a mixed sense. Most general is the bad habit of calling every inflammation of the throat with hyperæmia and yellowish spots diphtheritis, as well as applying the term diphtheritis to affections altogether different histologically. It is also hardly an advantage to call, with BRETONNEAU, the known specific throat affection "diphtheria," and then again to apply to the yellowish deposits upon or within the mucous membranes, etc., the word diphtheritis.—Consult VIRCHOW (*Arch.*, 1847, I., p. 253), BRETONNEAU (*Arch. gén.*, 1855), the Author (l.c.), ROSER (*Arch. d. Heilk.*, 1869, X , p. 103), SENATOR (*Virch. Arch.*, 1872, LVI.).

Croupous and diphtheritic exudations are PRIMARY and SECONDARY. The above views concern especially the primary of these forms of exudations. Secondary exudations are found in the same localities, besides in the mucous membrane of the œsophagus, vagina, urinary bladder, gall-bladder, perhaps also of the stomach, intestinal canal, etc.

The question concerning the IDENTITY OF THE DIPHTHERITIS OF WOUNDS AND THAT OF THE THROAT, and of other mucous membranes, is still open. External appearances, course, origin, and microscopical examination differ in many respects in the two affections. Inoculations furnish sometimes positive, sometimes negative results.

RECKLINGHAUSEN (*Virch. Arch.*, L., p. 552) inoculated fresh necrotic material from a patient with hospital gangrene into the cornea of a rabbit, and thereby produced a diphtheritic keratitis. NASSILOFF (*Ib.*) obtained negative results. According to HEIBERG (*Virch. Arch.*, 1872, LV., p. 257), croup and diphtheritis of wounds is a coagulation of pus, and a necrosis; hospital gangrene is a serpiginous necrosis. Consult, on the opposite side, EBERTH.

In late years the OCCURRENCE OF FUNGI IN DIPHTHERITIC EXUDATIONS has been almost constantly observed. The kind of fungus even is not yet well established. Besides, there still arise differences of opinion concerning whether the fungus is only accidentally present, or whether it is the essential cause of the local and general disease not infrequently connected with it : the former appears to be the case from investigations on man, the latter from the numerous experiments by inoculation on animals. In man, fungi (micrococcus, vibrio, leptothrix) occur constantly in the uppermost layers of laminated epithelium. They are found mostly as masses of globular bacteria, regularly also in the uppermost layers of not quite fresh croupous and diphtheritic deposits.

According to BUHL (*Z. f. Biol.*, 1868, III., p. 341), a fungus constantly occurs in diphtheria, which grows through the epithelial layer of the mucous membrane. B. leaves undecided whether the fungus is peculiar and necessary to diphtheria, or whether it is accidental—the *leptothrix buccalis.*

According to NASSILOFF (l. c.), development of fungus is primary in diphtheritis, and is the cause of necrosis. Diphtheritic membranes contain fungi constantly ; the latter appear on the borders of the changed parts in the epithelium, even where no membrane is yet formed ; they penetrate deeply into the tissue, following the passages of the juices and lymphatics. According to N., the form of the meshes of the net-work changes with the nearer approach to the free surface of the diphtheritic membrane. The former, and the pus-corpuscles lying in it, contract, and on the

surface the latter corpuscles disappear almost entirely. The brightness also of the fibres disappears, between them the meshes become almost invisible, because they are filled with granular brownish masses (fungi). These masses increase always upon the surface to quite thick layers, whilst they form scattered flat masses or sharply defined spheres. From the surface of the membrane the fungi penetrate deeply in striæ and by degrees disappear; many of these fungus-globules, however, are found also in the lowest layers of the membrane. Fungi are found within the peculiarly formed epithelium, most abundantly in the nucleus and around it; they decrease toward the periphery, but occur also in the thick cell-processes. NASSILOFF found on the mucous membrane of the nose and throat of a diphtheritic person a brown mass, consisting of fungi. Here and there, especially in the mucous and sub-mucous tissue of the larynx, in another case, the plasmatic canals of the connective tissue as well as the lymphatics were filled with fungi. In the former case the vomer showed forms similar to the lacunæ of Howship as well as Haversian canals, entirely filled with fungi. They had also penetrated throughout the basis substance of the cartilage: the contours of the cartilage-cells were indistinct and finally disappeared entirely.

NASSILOFF (*Ib.*) inoculated diphtheritic matter from the throat and larynx into the cornea of a rabbit. Already on the first day there appeared at the point of inoculation a clouding, and a reddening and purulent secretion of the conjunctiva. By microscopical examination of the cornea on the second or third day after inoculation the point of the operation and its vicinity was found to be gray or light brown: the plasmatic canals were filled in various degrees with fine fungus-masses, so that, in a few cases, between them only a small part of the surface was perceptible. Farther away in the neighborhood of this point the plasmatic canals were filled with pus-corpuscles, the cornea here being pure white. N. found these fungus-masses and those from diphtheritic membranes in man microscopically and micro-chemically identical.

Consult also LETZERICH on exudation and pus-formation (croup and diphtheritis) in the organs of respiration (*Virch. Arch.*, XLV., p. 327 *u. s. w.*; LIII., p. 493), and CLASSEN (*Ib.*, LII., p. 260).

According to EBERTH (*Zur Kenntn. der bacterit. Mykosen*, 1872), in diphtheria, fungi settle first upon the epithelium of the corresponding mucous membranes, or upon the surfaces of wounds, and later pierce successively the deeper layers of epithelium, then the mucous membrane and the neighboring tissues, to the destruction even of firm parts, like bone and cartilage. The passages for this extension are especially the lymphatics and fissures in the tissue. From here the fungi pass through the walls even of the larger bloodvessels into the circulation, and are the cause partly of septicæmia, partly of capillary embolisms of the renal glomeruli, of the liver, etc., with secondary formation of abscesses. The character of diphtheria is most probably a mykosis; bacteria are the bearers of the contagion.

Most INOCULATIONS of croupous and diphtheritic matter have been made with regard to the fungus character of the diseases in question. As it appears, the disease may be really induced through such inoculations into the corresponding organs.

TRENDELENBURG (*Arch. f. klin. Chir.*, 1869, X., p. 720) inoculated fifty-two animals, especially rabbits, mostly upon the trachea opened from without, into which he commonly introduced croup-membrane from men recently dead. In eleven cases (rabbits and doves) macroscopically and microscopically characteristic croup-membranes were found about 25 mm. into the tissue about the wound; the mucous membrane had always undergone extensive purulent infiltration. When four equally large rabbits had been in the same manner inoculated with the same material, it frequently happened that one sickened with all the symptoms of croup, and after death showed distinct formation of membrane, while the second showed only ecchymoses in the mucous membrane, the third was affected by only a severe catarrh, and the fourth retained a completely intact mucous membrane. The condition was the same, when pieces of membrane had been sewed into the tracheal wound so as to prevent its being coughed out. That the croupous inflammation of the trachea was not caused by the mechanical irritation of the piece of membrane brought in contact with it, was shown by twelve experiments, where only catarrh, not formation of membrane, resulted. After tracheotomy various materials were introduced into the trachea (charpie, skin, caoutchouc, writing-sand). This is demonstrated also in those cases where foreign bodies (pearls, plum-pits, pieces of money, etc.) have entered the human trachea:

among thirty-four cases collated by the author, there never resulted croup, but only high grade of suppuration, bronchitis, or pneumonia.

OERTEL (*Bayr. Int.*, 1868, No. 31, and l. c.), by numerous systematic inoculations, has demonstrated that the process, which is developed after inoculation of diphtheritic substances into the skin and tissues, is an altogether specific one. He does not assume therefrom that the diphtheritic affection of the throat and air-passages is a secondary localization of a process of infiltration generally distributed over the whole body. The diphtheritic contagium acts much more where it acts first, destructively on the locality where it is situated, and penetrates thence into the lymphatics and tissues, until it destroys life secondarily through general infection, if it does not sooner kill by suffocation.

The ARTIFICIAL PRODUCTION of croupous exudations by other, especially chemical substances, is not yet certainly proven.

Many cases which may here be considered, as by injection of ammonia into the trachea (STRICKER-REITZ), resemble pure croup only on superficial examination. SOMMERBRODT (*Virch. Arch.*, 1872, LV., p. 165) has, by immediately repeated injections of fresh blood and sol. liq. ferri sesquichlor., as well as of the latter alone, into the trachea of dogs, produced " croupous pneumonia."

HÆMORRHAGIC EXUDATIONS

Are those which contain red blood-corpuscles in great quantity, for the most part in so great abundance that the color of the exudation thereby becomes a darker or lighter red. Therein the red blood-corpuscles are found either as almost the only element, or with a small quantity of serum, and with very few white blood-corpuscles: PURE HÆMORRHAGIC EXUDATION. Or, besides the red blood-corpuscles, these exudations contain serum (SERO-HÆMORRHAGIC exudations), or mucus (MUCO-HÆMORRHAGIC exudations), or fibrin (FIBRINO-HÆMORRHAGIC exudations), or pus (PURULO-HÆMORRHAGIC exudations); or they are croupous-diphtheritic (CROUPO-HÆMORRHAGIC exudation),—in fact, all possible proportions can occur between the blood and the second element of the exudation.

The CAUSES of hæmorrhagic exudations are not specially known. Their general causes lie at one time in the intensity of congestive hyperæmia, introducing every acute inflammation; at another time in special relations of structure of the inflamed organs, especially of those the capillaries of which are surrounded by a very soft and yielding tissue (the capillaries of the lungs and brain; the vessels of eroded and ulcerated parts of the skin and mucous membranes, the vessels in many inflamed parts chiefly); finally, in unknown conditions of the vessel-wall, or of the blood, or of the whole system (as in hæmorrhagic measles, scarlatina, small-pox, scurvy, hæmophilia, etc.—see p. 215), perhaps also in peculiarities of epidemics.

In hæmorrhagic exudations either the exit of the red blood-corpuscles and of the other elements of the exudation (serum, pus-corpuscles, etc.) takes place at the same time (as probably in croupous pneumonia, hæmorrhagic small-pox, many acute inflammations of the brain and kidneys); or the bleeding follows only after previous exudations of other kinds. The exit of blood itself results in various cases, probably in different ways: sometimes with laceration of the vessel-wall (*per rhexin*), sometimes without visible injury of the vessel (*per diapesin*—see p. 211).

With our present knowledge of the structure of the vessels and inflammation, the latter mode of bleeding no longer appears unintelligible. Also the frequent or constant occurrence of red blood-corpuscles in many inflammations of the lungs (rusty sputa), of the brain (red inflammatory cerebral softening), of the mucous membrane of the intestines have been known a very long time. Many inflammatory diseases

may be exactly divided into those in which, besides blood-serum, the white corpuscles form the exudation; and into those, where, besides the former, red corpuscles form the exudation. So I find between the hæmorrhagic or black, and between the common or yellow pustules of *variola vera* on the skin and mucous membranes no other distinction than that the former contain only red, the latter only white blood-corpuscles within the cells of the rete Malpighii which have swollen up into large vesicles (*Arch. d. Heilk.*, 1868, IX., p. 505). Further, beneath the diphtheritic infiltrated mucous membrane of the throat appear croupous deposits, which in the spaces of the net work contain only red blood-corpuscles (*Ib.*, VII., p 481).

Sometimes the red color of an exudation does not depend upon escaped blood, but upon the coloring matter of the blood which has oozed through the vessels, as in many hypostatic and in asthenic inflammations.

See above concerning hæmorrhagic exudations having their origin in hæmorrhages from new-formed vessels.

NEW-FORMATION OF TISSUES IS THE THIRD ESSENTIAL PHENOMENON OF INFLAMMATION.

New-formation of tissues is much less constant than hyperæmia and exudation. It occurs especially after determined causes (wounds), in certain localities (endothelium, epithelium—skin and serous membranes), in the course of many chronic inflammations, as well as in consequence of degenerative or destructive processes in inflammation of almost every kind.

New-formed tissues resemble completely, or in essential points, normal tissues; or they deviate from them. In the former case the new-formation of tissue is represented as a regeneration of epithelium, connective tissue, osseous tissue, etc., or as cicatrices, as inflammatory hypertrophy or induration, or as pseudo-membrane. New-formed tissues themselves are oftenest epithelium of every kind, and glandular cells, as well as endothelium; also frequently (and in most all parts) connective tissue with vessels or (near the bones) osseous tissue; in some tissues, which consist of cytogenic substance, it is the latter. In rarer cases there arise tubercle, carcinoma, and other heteroplastic new-formations.

The new-formation of vascular connective and osseous tissue, that of epithelium, tubercle, cancer, etc., will be considered later. (Concerning desquamative inflammation *vide infra*.) But the formation of pseudo-membranes, which on serous, more rarely on synovial and mucous membranes, represent ADHESIVE INFLAMMATION, is usually considered as inflammatory, wherefore their consideration belongs here.

In adhesive inflammations of serous and synovial membranes there quickly appears on those membranes a very vascular granulation-tissue. The new formed vessels of the opposite wall of the serous membrane, etc., grow until they meet one another and blend. A part of the vessels recede while others become thicker-walled and wider. Simultaneously, connective tissue appears out of the granulation-tissue, which undergoes the common cicatricial contraction. Serous cavities and those of the joints are thus obliterated entirely or in part. The time within which a firm adhesion results is, from observations on man, and from experiments, two to three weeks.

The fibrin-like connective-tissue growth of serous membranes, until now called fibrinous exudation ,is, according to BUHL, the young growing connective tissue rising above the normal limits of those membranes. Perpendicular sections show : first, the swollen serous membrane provided with numerous granules ; then follows a vascular layer, which consists of round or spindle-shaped cells, and of nuclei as well as of a distinctly fibrous or homogeneous intercellular substance ; uppermost lies a non-vascular layer. poor in cells, consisting of homogeneous fibrin. Upon this, endothelial

cells are found here and there, which show fatty or mucous metamorphosis, or nuclear proliferation. The two lower layers pass gradually one into the other, while the uppermost is separated from them for the most part by an even or irregular line. The existence of vessels, which are connected with the normal vessels, has been demonstrated by BUHL even in fresh exudations by artificial injection of them. The vessels in the dead body are mostly empty, giving the fibrin-like appearance of this desmoid tissue. The uppermost layer, according to BUHL, is like that lying under it, but without vessels, and with but few cells.

Besides the desmoid fibrin the serum present is the peculiar exudation, and comes mostly from out of the new-formed vessels : so much the more as these vessels in part describe greater and greater excursions, are permeable, and therefore the blood-current in them is greatly retarded. From out of this serum, in many cases, fibrin separates through contact, e.g., with the air, and commonly floats loosely in the liquid. At other times the fibrinous coagula of the surface proceed from wounds, laceration of the vascular layer, and extravasation of fibrin. Most frequently the fibrin appears to be the product of the new-formed vessels themselves.

HÆMORRHAGIC EXUDATION of serous membranes proceeds usually from rupture of the uppermost extremities of the new-formed vessels of the desmoid fibrin. The blood penetrates partly the fibrinous exudation itself, partly flows over this into the serous transudation. If the vessels are torn at their base, which is very rare, they separate the fibrin by pieces.

In mucous membranes the same growing together of opposite parts happens if the epithelium is destroyed, and the tissue of the mucous membrane is changed into vascular granulation-tissue.

New-formation of connective tissue in PARENCHYMATA is represented by indurating inflammations, in which inter-acinous, inter-lobular, etc., connective tissue increases in quantity, while the peculiar parenchymatous tissue remains at least normal in amount. If, in consequence of cicatricial contraction of new-formed connective tissue, the parenchyma loses its vascular and glandular constituents, the organ grows smaller and at the same time becomes indurated; inflammatory indurative atrophy, cirrhosis, etc. Both conditions are most prominent and oftenest found in the liver and kidneys, less often in the mammæ, salivary glands, lungs (chronic interstitial pneumonia). Their causes are sometimes unknown, and sometimes known, as, e.g., the habitual use of alcohol as the cause of granular liver.

Many of the new-formations mentioned appear at one time with inflammatory phenomena, at another time not, so that the same processes can be referred as well to chronic inflammation as to non-inflammatory connective tissue hypertrophies. Thus, many scleroses of the skin and mucous membranes, many pulmonary, hepatic and renal indurations, gray degeneration of the posterior columns of the spinal cord, etc.

A NEW-FORMATION of CYTOGENIC TISSUE in consequence of inflammation, is not infrequently observed in the solitary follicles of the mucous membrane of the throat and intestines, in the tonsils and lymphatic glands. It affects sometimes only the purely cellular parts, sometimes at the same time also the delicate stroma, whereby lasting hypertrophies often result, sometimes only the stroma and the common sheath-walls of connective tissue.

RETROGRESSION, OR DEGENERATION FORMS THE LAST CHIEF PHENOMENON OF INFLAMMATION.

DEGENERATIVE PROCESSES are present in every inflammation. In the first rank are to be mentioned changes of the vessel-walls, which render possible the passage through them of a more abundant liquid, which is often of a different nature, as well as of white, and not infrequently of red blood-corpuscles, without the microscope being as yet unable to discover any interruption of structure. The inflammatory changes of many other tissues are more exactly known. These changes are frequently so SLIGHT that the

tissues may, in spite of them, return again to the normal state. Sometimes, only or chiefly, they consist in changes of form: as in epithelial and in glandular cells which present the most manifold changes of form. Or, the changes are of chemical nature. These consist oftenest in albuminous infiltration, which, if not of too high grade, (probably also the slight degrees of serous infiltration and of fatty metamorphosis,) may revert entirely to the normal state. The endothelium, e.g., of the serous membranes, and the epithelium of various mucous membranes, the peculiar gland-cells present in every inflammation one or another of these changes. Mucous metamorphosis of various epithelia of mucous membranes is never absent in inflammation of them, but is distinguished in no essential point from those occurring normally. Finally, catarrhal inflammations are here to be mentioned, where besides increased production of mucus and under slight suppuration the epithelium is either not destroyed at all, or not to its lowermost layer, and in the latter case it is quickly regenerated.

At other times, however, the degenerative processes of inflammation are so INTENSE that it is no longer possible for the tissues to recover their normal state. These processes are the higher grades of albuminous and serous infiltration, of fatty and croupous metamorphosis, of mucous softening. They affect cells of every kind, especially epithelial and gland-cells, fibres, such as muscle and nerve-fibres, basement tissues, such as those of connective tissue, cartilaginous and osseous tissue. The tissues affected are destroyed in consequence of such degeneration, and it depends further upon the kind and duration of the inflammation, upon the kind of tissue affected, upon the adjacent tissues, etc., whether the tissues can be regenerated, as is the case with most epithelia and endothelia, sometimes with muscle-fibres, osseous tissue, or whether a permanent defect is engendered, as in glandular and nerve-tissue. Further, in this connection belong the recently directly observed transformation of persistent cells, e.g., connective-tissue corpuscles, corneal corpuscles, into movable cells, with their final destruction, or with their increase, and transformation into pus-corpuscles.

Degeneration in inflammation is most distinct in many epithelial tissues, inclusive of gland-substance, in adipose tissue, in the brain and spinal cord, in muscular, and in osseous tissue. Besides, it preponderates in many chronic inflammations where, besides a new formation of connective tissue, there is often present a destruction of the inclosed elements of glandular or nervous nature.

In inflammation of the bones there is developed from the connective tissue of the external surface of the vessels, and from the granulation-tissue of the marrow, few or abundant pus-corpuscles: this tissue induces, through pressure on the one hand, through diminished blood supply on the other, a consumption of the bone-substance in form of regular or irregular lacunæ. In place of bone-corpuscles are found pus-corpuscles, and with their increase the spaces in which the bone-cells lie increase in size; sometimes so that the corpuscles and processes become wider, sometimes, and for the most part, round cavities, as if chiselled out, are present in place of the previous bone-corpuscles. These cavities, first described by HOWSHIP, have their origin, according to VIRCHOW, FÖRSTER, etc., in a disturbance of nutrition of the osseous frame-work acting upon the bone-corpuscles; according to BILLROTH they are the results of the mechanical action of the granulation-tissue, and appear as in living bones, also in experimentally inclosed dead bones, and in pegs of ivory. The names more or less in use for these degenerative bone-inflammations are: rarefying ostitis, fungous ostitis, fungous caries, inflammatory osteoporosis.

A number of degenerative inflammatory forms in soft parts, as well as in bones, pass with no sharp boundary into GANGRENE. Theoretically, both

processes are altogether different; but practically, manifold intermediate grades are observed, ætiological, pathologico-anatomical, and clinical.

In many places inflammation is attended with degenerative and neo-plastic processes in immediate connection with each other; as in atrophic increase of fat, in polynuclear bone-cells.

SYMPTOMS OF INFLAMMATION.

The four cardinal symptoms (redness, heat, swelling, pain) and disturbances of nutrition are demonstrable only in acute inflammations, most successfully in inflammations of the skin and subcutaneous cellular tissue, as well as of mucous membranes externally accessible, and of the membranes of the eye. In all other parts two or three of the symptoms named must suffice for the diagnosis.

The redness of inflammation resembles in general the redness of congestive hyperæmia, but is usually more intense and of longer duration.

The swelling varies with the degree of hyperæmia, with the kind and quantity of exudation, with the locality, with the kind of inflamed tissue or organ, so that a general representation of it is impossible.

The pain is especially severe where the parts are abundantly supplied with sensitive nerves, and where the inflamed part is prevented from expanding (inflammation of the tooth-pulp, suppuration under the nail, under the skin of the finger, under fascia, under periosteum; inflammation with sudden swelling of many glands). Many inflammations of the skin, and especially of mucous membranes, are attended by little pain, many are entirely painless. Those of serous membranes are in part very painful. The severity of the pain here in most cases stands in direct ratio to the intensity of the inflammation. The pain sometimes continues uninterruptedly, sometimes it is attended by exacerbations, and is irregularly, seldom regularly intermittent. It is of the most different quality, in external parts not infrequently beating and pulsating, at other times tense, burning, etc.

Pain affects sometimes only the parts inflamed; sometimes it is present in the whole length of the nerve of the part (suppuration in the finger), sometimes it radiates to other branches of the same nerve (toothache to many branches of the trigeminus). Sometimes the cause of pain is not known: in inflammation of the testicle pain along the inner surface of the corresponding thigh; in inflammation of the hip-joint, pain in the knee; pain in the left shoulder in inflammation of the heart; in the right shoulder in inflammation of the liver.

The pain of inflammation is explained by the conditions of pressure and tension, and probably by minute, but still unknown, changes at the extremities of the nerves.

The HEAT OF INFLAMMATION, LOCAL ELEVATION OF TEMPERATURE, is NOT INFREQUENTLY only subjectively distinct: yet is it perceived by the sick for the most part only in inflammations of external parts, rarely in those of internal organs. But it is often present also OBJECTIVELY. Its degree is usually in proportion to the intensity of the inflammation. It is mostly continuous. Accurate thermometric investigations have shown that the TEMPERATURE OF INFLAMED PARTS AT THE PERIPHERY IS USUALLY LESS THAN THAT OF THE INTERNAL PARTS OF THE BODY; ON THE OTHER HAND, IT IS CERTAINLY HIGHER THAN THAT OF THE CORRESPONDING HEALTHY PART. The CAUSE lies partly in the increased quantity of blood in the inflamed organ,

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partly perhaps in an increased transformation of its tissues. And yet there are also many contrary statements.

At the focus of inflammation, not only the temperature is actually raised objectively, but also its POWER OF RADIATION has increased. That cold applications on inflamed parts very soon become warm, that with ice even the local heat is hardly lessened, is taught by daily experience. HUNTER found the warmth in inflamed parts in animals and man generally not higher than in internal parts. Since more arterial blood flows into inflamed parts, and in fever a more heated blood, so parts of the skin which are accustomed to a cooler temperature are felt to be insufferably hot. BÄRENSPRUNG also demonstrated the radiation of heat, when he found that the thermometer made an average rise of 1° in 0.7 minutes (as in fever), and that in inflammations of the skin during the first minute it rose to 8.6 (still more than in fever, where it amounted to 6.9°).

But if in the inflamed parts more heat is produced than during ordinary tissue-changes, so this increase may be slight and on this account hardly measurable; because in a part pierced by so many channels with movable liquid, a temperature independent of that of the blood can hardly be retained, regardless of the greater cooling off toward the exterior. But HUNTER really found in some cases, e.g., in the tunica vaginalis of the testicle immediately after operation for hydrocele, the temperature of the tunic 33.3 C., on the following day 37.1 , a rise of almost 4 C. BECQUEREL and BRESCHET also found, by means of thermo-electric measurements, in inflammatory swellings elevations of 1–2° and more in contrast with normal skin and muscle.

J. SIMON (HOLMES, *Syst. of Surg.*, 1860, Art. "Inflamm.," p. 43) found by thermo-electric measurements, that arterial blood flowing into an inflamed extremity is less warm than the focus of inflammation itself; that venous blood flowing from the extremity is less warm than the focus of inflammation, but warmer than the blood from the corresponding arteries; that THE VENOUS BLOOD IS WARMER THAN THAT OF THE CORRESPONDING HEALTHY SIDE OF THE BODY.

BILLROTH and HUFSCHMIDT (*Arch. f. klin. Chir.*, 1864, VI., p. 373) found in 37 comparative measurements of the heat in a wound and in the rectum, that in 28 the temperature was lower than that of the rectum, in 8 the temperatures of both parts were equal, in 1 that of the wound was 0.3 higher.

O. WEBER'S experiments (*Deutsche Klin.*, 1864, No. 43 et 44) showed, that the temperature of an inflamed part may exceed that of a part in which it is raised through paralysis of the vaso-motor nerves and the resulting fluxion. W. measured the temperature in inflamed parts in 8 animals (of these 7 were dogs) 31 times: in 9 the heat of the wound was greater, in 15 less, and in 6 equal to that of the anus. In all these experiments the thermometer was applied only to the surface of the wound, at the most beneath the borders of the wounds. W., like SIMON, also compared the temperature of the instreaming arterial blood, as well as that of the outflowing venous blood, with that of the focus of inflammation itself and then with that of the corresponding healthy parts: in all 6 cases the temperature within the rectum was lower than that in the inflamed part of the fracture, or that of the parts surrounding the wound or even that of the wound itself. W. corroborated SIMON's results in other respects.

JACOBSON and BERNHARDT (*Med. Ctrlbl.*, 1869, No. 19) excited inflammations of the pleura or of the peritoneum by subcutaneous injection, and by means of thermo-elements compared the temperature of the affected with that of the uninjured serous sacks, as well as with that of the right or left side of the heart. (Normally, the pleural sacks are as a rule about 0.1–0.2 C. cooler than the abdominal cavity, and 0.2–0.5° C. cooler than the left side of the heart.) They found that WITHOUT EXCEPTION THE TEMPERATURE OF THE INFLAMED PARTS WAS LESS THAN THAT OF THE HEART.

LAUDIEN (*Med. Ctrlbl.*, 1869, No. 19), in 40 observations on dogs and rabbits by the electric method (WIEDEMANN's mirror-galvanometer), found the following: The temperature of the skin or of muscles inflamed to a high degree, to their deepest layers in the immediate neighborhood of the bones, never reaches that of the interior of the body: the difference in very intense processes still almost always amounts to 1–2 C. The temperature of an inflamed part in the acute stage usually exceeds that of the corresponding healthy part, if by communication with the atmosphere (open wounds and ulcerations) a continuous loss of heat has not been sustained. The difference lessens with the distance of the tissue from the surface:

in the inflamed ear of a rabbit, 4 and 5° C. ; in the inflamed deeper muscles of the extremities of dogs and rabbits, seldom 1 , mostly 0.2–0.5 C. In the further progress of inflammatory processes, in extended purulent infiltration or abscess in deep parts, the analogous part of the healthy extremity is sometimes found warmer. The temperature of the arterial blood (art. cruralis in dogs) was higher than that of the focus of inflammation, which it supplied. (Consult also JACOBSON, *Virch. Arch.*, LI., p. 275.)

SCHNEIDER (*Med. Ctrlbl.*, 1870, No. 34) after many measurements in man, confirmed HUNTER'S statements, that the elevation of temperature of inflamed organs was due only to the heat introduced by the inflowing blood-current, not to that formed in the tissues.

HUPPERT (*Arch. d. Heilk.*, 1873, XIV., p. 73) found the temperature of the dropsical cavity of the tunica vaginalis to be 35 C. After mechanical irritation it rose to 1.5–2.5 , thus exceeding the normal blood-temperature not more than 0.5 at the most. Almost simultaneously with this local elevation, the general temperature also rose ; the latter was absolutely always higher than the simultaneous local temperature. The local temperature harmonizes with the general ; but the variations in the course of the latter always precede those of the former.

The FUNCTION OF INFLAMED PARTS is almost always more or less DISTURBED. The disturbance is manifest in proportion to the knowledge we have of the function, and the ease with which it can be demonstrated. Function is either LESSENED or altogether destroyed : an inflamed cornea is less transparent ; an inflamed bone is for the most part incapable of use ; an inflamed muscle does not contract ; an inflamed gland does not perform its function, or does so incompletely, etc. Or the function is CHANGED, which is made known especially by the appearance of involuntary reflex movements : thus in different inflammations of the eye there appears spasm of the lids, in inflammation of the nasal mucous membrane sneezing, in those of throat swallowing, in laryngeal catarrhs, changes of the voice and hoarseness, in catarrhs of the air-passages chiefly cough, in inflammation of the rectum tenesmus, in those of the urinary bladder spasm of the bladder. In very many peculiar ways is the change of function in the nervous system made known, as well in respect to psychical action as to motion and sensation. Disturbance of function is certainly an important symptom of inflammation, but it also belongs to all other local disorders of nutrition.

If heat, redness and swelling make known inflammation in external parts or in parts opening externally, with respect to the diagnosis of inflammation of internal organs, no information is furnished in many cases either by disturbance of function, or by pain and heat, to say nothing of swelling and redness, which cannot be seen. There result, instead, in individual organs, a series of important symptoms from mechanical conditions, which become changed during the course of inflammation. The ducts of mucous membranes become narrowed by exudation and by hyperæmia, which in some cases at least affords distinct symptoms : thus in catarrh of the nasal and urethral mucous membrane, in that of the mucous membrane of the air-passages, especially of the glottis and small bronchi. In cases of intense inflammation of serous and mucous membranes, not only the serous and subserous, the mucous and submucous, but often also the subjacent muscular tissue is infiltrated by serum and is thereby in varying degree paralyzed : thereon depends, *e.g.*, the protruding of the intercostal spaces in pleuritis, paralysis of the heart in pericarditis, in part the dyspnœa in croupous laryngitis, diminished peristaltic movements of the stomach and intestines, meteorism, sometimes prolapsus, invagination of the intestine in severe affections of the mucous or serous membrane. In the lung, parts previously containing air become, through the exudation, empty of air, dense, firm, and furnish a different sound in auscultation and

percussion. Percussion and auscultation detect similar changes in inflammation of most serous membranes, if the exudation is scanty and firm, or abundant and of any consistency. In the heart the valves and orifices become changed by inflammation and its consequences, and after the valves cease to close or the orifices become too narrow, there arises a series of symptoms which are perceptible to sight, feeling and hearing. Inflammations of the remaining, especially parenchymatous, organs, which are not, or only in part, accessible to percussion and auscultation, are diagnosed partly by the presence of one or another of the five cardinal symptoms, partly by ætiological events, partly by the feverishness of the process and by the acuteness of its course.

Many inflammations furnish at no time of their course local symptoms: e.g., many of the brain and its membranes, lungs, heart, etc. Or, the symptoms are not to be distinguished from those of hyperæmia, hæmorrhage, gangrene, new-formations, etc., of the same parts.

GENERAL SYMPTOMS OF INFLAMMATION are absent in inflammations of slight extent and intensity, but otherwise they are always present. The blood of those sick with inflammation is characterized by absolute and relative increase of fibrin, and by the formation of the BUFFY COAT in the liquid drawn from a vein. The conclusions, which were formerly drawn from the presence of this layer with respect to the existence of inflammation chiefly, and from the extent, thickness, and firmness of the former with respect to the intensity of the latter, have not been found to stand the test, since that crust occurs also in affections not inflammatory.

FEVER is found in many inflammations, i.e., a marked rise of the temperature of the body, an increased frequency of the pulse and respiration, etc. This is generally in proportion with the extent and severity of the inflammation, but in special cases there are numerous exceptions. It was for a long time believed that fever depended upon the rise of temperature at the focus of the inflammation; but the quantity of heat here generated is in no case adequate, and is for the most part less than the temperature of the blood. And yet fever is of high diagnostic value with respect to the diagnosis of inflammations of internal parts.

The relative experiments of BILLROTH-HUFSCHMIDT, WEBER, FRESE, STRICKER, and others will be spoken of in Fever.

STRICKER (Stud. aus d. Inst. f. exp. Path., 1870, p. 31) found that excised tissues (e.g., the cornea of the frog) implanted on an inflamed part (into the folds of the nictitating membrane after previous cauterization of the cornea so as to penetrate through it), exhibited the peculiar inflammatory changes of the elements of the tissue: sometimes there were found only transformed corneal corpuscles, wandering cells in usual number, sometimes dense accumulations of smaller amœboid cells, besides more or less transformed corneal corpuscles.

Besides, there frequently appear still further general symptoms of inflammation, according as one or another of its aspects preponderates; e.g., in prolonged suppuration general anæmia and exhaustion of the organism (also hectic fever), fatty degeneration of the liver, spleen, kidneys, etc.; in many suppurations, especially acute suppuration of the bones, pyæmia, etc.; in diphtheritic exudations, severe general phenomena, paralyses, etc.

THE TERMINATIONS OF INFLAMMATION are DISCUSSION or RESOLUTION, DEATH, or in PERMANENT DISTURBANCES OF NUTRITION. Death may be local, GANGRENE; or GENERAL, death of the individual. Gangrene appears, if nutrition is wholly arrested. Death of the individual has different causes: in respect to the kind of inflamed organ, kind and extent of the inflamma-

tion, individuality, etc. The permanent disturbances of nutrition are ADHESIONS and INDURATIONS of organs, further DEGENERATIONS, which, strictly considered, still belong to inflammation. The same is true of the commonly developed SUPPURATION and ULCERATION.

DIVISION OF INFLAMMATIONS.

The phenomena of inflammation are in general, and with respect to their causes, the organs which they affect, their intensity and extension, etc., so manifold, that in the individual case not only the question is important, whether an inflammation is present, but also that a knowledge of its causes, of the preponderance of single principal phenomena, etc., is of the greatest interest. Inflammations are thus usually distinguished (besides, with respect to their duration: acute and chronic inflammations) from ætiological and from anatomical standpoints, as well as by their character.

I. ÆTIOLOGICAL DIVISION.

1. TRAUMATIC INFLAMMATIONS are the simplest, because they are usually developed in a previously healthy body, and because their causes are usually apparent, in part also because they can be more or less easily removed. Here belong especially SIMPLE or PURE WOUNDS. (*Vide* Repair.)

In CRUSHED and LACERATED WOUNDS the process is much less simple, because it is at the same time concerned with resorption of bloody effusions, with separation of dead parts, sometimes also with their absorption with participation of the whole organism, etc.

INFLAMMATIONS excited in various tissues and organs by FOREIGN BODIES are traumatic, in the wider sense; from such upon the conjunctiva and cornea, in the mouth, nose, air-passages, and lungs; besides, catarrhs arising from artificial teeth, stumps of teeth, etc., in the mouth, catheters in the urethra, pessaries in the vagina, in the rectum, etc. Urinary and biliary calculi sometimes exert the same influence on the organs where they are formed.

2. TOXIC INFLAMMATIONS. Inflammations caused by animal and vegetable PARASITES (fleas, lice, bugs, micrococcus, etc.: PARASITIC INFLAMMATIONS), also those excited by insects, etc., form the transition from traumatic to toxic inflammations. Besides, to this class belong those generated by CORROSIVE SUBSTANCES, which act upon the skin as well as upon mucous membranes. Injuries of the skin are caused accidentally by nitric acid, sulphuric acid, caustic lime, strong alkalies, etc. We excite the same process artificially to destroy and remove organic parts. Finally, acids and alkalies are sometimes taken into the mouth and stomach accidentally, sometimes with the intent of suicide. In the same rank are lunar caustic, corrosive sublimate, chloride of zinc, etc.

Also in this class are included inflammations which are the results of high degrees of cold and heat.

To toxic inflammations in the broader sense belong those which have their origin in irritation of the tissues by the blood after the entrance of POISONS into the blood, *e.g.*, urticaria in many after ingestion of various substances, mercurial stomatitis, etc.; chronic-gastritis, and granular liver from the habitual use of alcohol, as well as from phosphorus, nephritis from active diuretics. The peculiarities of these inflammations lie partly in their preference for certain parts of the body (that of mercury for the mucous membrane of the mouth, that of iodine for the skin of the face and nasal mucous membrane); partly in the preponderance of individual

elementary processes (in that from mercury great serous swelling of the tissues and exudation according to the kind of secretion ; in that from iodine, congestion, etc.).

Finally, to this class belong inflammations arising from abnormal chemical processes within the organism : catarrhal stomatitis of infants, many inflammations of the urinary bladder from retention and decomposition of the urine, pneumonia in bronchiectasis.

3. DYSCRASIC INFLAMMATIONS likewise have their origin through irritants, which are carried by the blood, and are thus in many ways connected with those just mentioned. Here great differences are found in individuals. (See Syphilis, Scrofulosis, Scorbutus, etc.)

Acute endocarditis is found especially in acute rheumatism of the joints, and in pyæmia. Consult HESCHL (*Oestr. Ztschr. f. pract. Heilk.*, 1862, Nos. 12 *et.* 13).

4. METASTATIC INFLAMMATIONS arise partly from emboli and collateral hyperæmia at the obstructed part, partly from an irritant in the blood, as in many cases of pyæmia. They occur chiefly in the lungs, liver, spleen, kidneys, serous membranes. They always attack parts which are confined and often wedge-shaped, but usually many parts in one organ.

The cause of orchitis, mastitis, etc., occurring particularly in epidemic parotitis, has heretofore in no manner been explained.

5. RHEUMATIC INFLAMMATIONS. The more immediate processes herein concerned are still unknown. Sudden cooling or wetting, especially of the body while perspiring, is the cause of inflammations belonging to this class, as many forms of erysipelas, angina, pneumonia, inflammations of the joints, etc.

6. Inflammations arising in consequence of CONTAGIONS and MIASMS are likewise altogether unknown with respect to their origin. To this class belong inflammations of the skin, mucous membranes of the eyes and nose in measles ; those of the skin, mucous membrane of the mouth and throat, sometimes also of the kidneys, in scarlet fever ; those of the skin and of many mucous membranes in small-pox ; those of the air-passages in whooping-cough ; epidemic diphtheritis of the mouth and throat ; mumps ; inflammations of the mucous membranes and muscles in glanders, etc.

Many SECONDARY inflammations are, with respect to their more immediate cause of origin, wholly unknown : stomatitis in severe acute and chronic diseases, pericarditis in carcinoma, etc.

7. HYPOSTATIC INFLAMMATIONS arise slowly from hyperæmia in which the weakened heart's action (in acute and chronic marasmus), the disposition, a pressure from without upon the skin, or in the bronchi, lungs, urinary passages, the remains of products of secretion act as the irritants. The redness is mostly dark, livid, and dependent upon injection as well as upon imbibition ; the exudation is slight, more of the serous variety ; new-formations are mostly absent, and destruction depends mostly upon maceration and necrotic processes (bed-sore).

II. CLASSIFICATION OF INFLAMMATIONS ACCORDING TO THE PREPONDERANCE OF SOME ONE OF THEIR ELEMENTARY PHENOMENA.

1. Congestive or vascular forms of inflammation.

Their chief factor is congestive hyperæmia. Symptomatically, redness and swelling are shown, which are dependent upon hyperæmia, and upon serous, or mucous, or sero-purulent exudation, for the most part simultaneously present; later sometimes also upon elongation of the vessels and proliferation. New-formation and retrograde metamorphosis are wanting entirely, or show only a slight development. Complete return of the inflamed tissues to the normal state is the rule.

Congestive inflammation is the oldest form of inflammation. It is best represented by inflammations of the skin, if they are acute and terminate with healing: erythema (common, or in scarlatina), erysipelas, phlegmons; as well as by inflammations of the mucous membranes which are characterized as acute catarrhal, with or without slight secretion, or as phlegmonous forms: conjunctivitis, stomatitis, gastritis, enteritis, bronchitis, etc. Erythematous inflammations of the skin and mucous membranes affect the upper, phlegmonous inflammations affect the deeper layers of the skin and mucous membrane, sometimes also the subcutaneous, i.e., the submucous and inter-muscular connective tissue: the exudation is mostly slight, sometimes it is more abundant or it proceeds to the formation of pus (e.g., in the gums: so-called parulis). Also the lightest and most transient forms of inflammation of the serous membranes (pleuritis, peritonitis, meningitis) and the simple acute inflammations of the glands (orchitis, mastitis, parotitis, nephritis, many inflammations of the lungs) belong to this class.

The so-called congestive inflammations, which furnish manifold transitions to non-inflammatory congestion, sometimes often return in the same individual, even many times, for the most part, with irregular intermissions; sometimes also regularly in short (daily) or longer (monthly) periods. Similar conditions are found in many inflammations of the same kind with serous exudation: e.g., many such regularly recurring inflammations of the joints have lately been observed.

Many mucous membranes, e.g. that of the larynx, are in the dead body always pale even in congestive forms of inflammation, because of their abundant elastic fibres; but in the living, redness of the parts, with the exception of the vocal cords, may be very intense.

2. Exudative forms of inflammation.

These are characterized by the quantity and peculiarities of the exudation. They presuppose always a more or less great participation of the vessels.

a. Inflammations of serous membranes with fibrinous exudation are the purest of these forms. In mixed exudations, or those containing a large quantity of fibrin, the exudation, in contrast to the vessel-changes, appears in the foreground, especially if they are secondary, i.e., if the inflammations are caused by an irritant from the blood: as in pyæmia and puerperal fever, when for the most part a large quantity of serum and fibrin are exuded with slight vascular changes. If these inflammations are primary, arising from cold ("rheumatic"), the vascular changes are, besides the exudation, distinctly visible. If they are traumatic, caused, e.g., by perforation of the intestines, vascular changes appear very early and are strongly developed. It is to be observed symptomatically, that the pain appears to be severe in proportion to the hyperæmia and vascular disturbance, so that inflammations of serous membranes from perforation are the most painful, those from colds less so, those occurring secondarily in pyæmia the least, or give rise to no pain at all. Inflammations of mucous

membranes and of the skin rarely occur with exudation.   (See Croupous
Exudation.)

b. Inflammations with SEROUS EXUDATION are differently formed according
to the seat of the exudation.   It passes out of the vessels quickly through
the epithelium or endothelium to the surface of the affected membrane,
without any essential change in the former : in many acute serous exuda-
tions of serous and synovial sacs ; in many inflammations of mucous mem-
branes, with abundant serous or sero-mucous, or at the same time slightly
purulent exudation (many forms of stomatitis, bronchitis, intestinal catarrh,
also, in part, cholera) ; in many parenchymatous inflammations (lungs,
kidneys).

RADZIEJEWSKI'S investigations on the action of cathartics show that transudation
does not come into play, but only the increased peristaltic movements (whilst the
blood in the intestinal wall, by taking up the cathartic, contains its peculiar irritant).

If the epithelium does not allow such a passage through of the exudation,
the uppermost impermeable epithelial layer (epidermis, uppermost layer of
laminated epithelium, as of the œsophagus, urinary bladder, etc.) rises up
in the form of a vesicle (blisters, also in part the vesicles of herpes, of
erysipelas, and of pseudo-erysipelas, perhaps also of eczema, of varicella,
peculiar vesicles of mucous membranes).   After the opening, artificial or not,
of the vesicle, the exudation either is arrested (blisters, herpetic vesicles)
or it still continues for a variously long time (vesicles of eczema).   At
other times the exudation fills out the cells, first of the middle, then of the
lower epithelial layer, and these distend to different degrees : there appears
on the surface of the skin or mucous membrane, first a papulous, then a
vesiculous elevation, which is finely partitioned, i.e., by epithelial strings,
which are not filled with exudation, but are drawn out, etc.   This is the
case in small-pox PUSTULES, in the cavities of which there afterward
appear white (or red) blood-corpuscles, upon the skin as well as upon the
mucous membranes ; in many vesicular eruptions of mucous membranes
provided with laminated epithelium.

If the serous exudation does not, or only in part, penetrate through the
cells of the skin or mucous membrane, its accumulation raises up sometimes
the uppermost, sometimes the deeper epithelial layers ; the lowermost layer
is rarely raised.   Thus arise the DESQUAMATIVE INFLAMMATIONS OF THE SKIN
AND MUCOUS MEMBRANES.   Those of the former occur in erythematous,
erysipelatous, scarlatinous, and eczematous inflammations.   In the colon
the separation of the epithelium may take place to such an extent and so
completely, that masses of it are evacuated, which under the microscope
are found to be only epithelium with pores for the mucous glands.

According to most authors, such a desquamation should take place in cholera ; but
examinations of the cholera stools of the living, as well as of the intestinal mucous
membrane soon after death, demonstrate the untenableness of this view.   The form
just given of desquamative catarrh of the colon, I saw in a case of colitis, which was
caused by a clyster of slightly diluted vinegar.

c. DESQUAMATIVE (or parenchymatous) INFLAMMATIONS OF PARENCHYMA-
TOUS ORGANS (lungs, kidneys, liver) consists in the swelling of the paren-
chyma by serous infiltration, and, in consequence, in a separation of the
epithelium.   The cells of the latter are enlarged, more rounded, and filled
with albuminous, and, in part, oily molecules.   They pass out either entirely

(in the kidneys with the urine), or partly (in the lungs by expectoration); or they remain in the cavity affected, either to become absorbed or to undergo cheesy transformation (see Cheesy Inflammations). These inflammations are either secondary (from poisons, in typhoid fever, acute exanthemata), or they are primary, and then pass by transformations of tissue into productive inflammations.

Consult BUHL, *Lungenentz*, u. s. w., 1872, p. 38. [Am. edition, 1875.]

In serous infiltrations of the skin and mucous membranes, and parenchymata, which are commonly called INFLAMMATORY ŒDEMA, the inflammatory character of them is often doubtful (œdema glottidis, cerebral œdema); they can then properly be called inflammatory only when congestive hyperæmia is present with hæmorrhages, and pus-corpuscles are found besides the serum. The most developed are those inflammations of the skin in many of the lighter phlegmonous inflammations, in the rectum in the comparatively severe forms of dysentery. To inflammations with serous exudations as a preponderating element, belong also many forms better known clinically than anatomically : epidemic parotitis, serous orchitis (especially in gonorrhœa), perhaps also many inflammations of the brain, lungs, and liver. Inflammations of this kind of the parotid glands and testicles have a great similarity with the retentions of lymph, which, *e.g.*, arise in the submaxillary glands, if the excretory duct be ligated and the nerve irritated.

d. MUCOUS INFLAMMATIONS are those inflammations of the mucous membranes in which mucus preponderates and is produced in greatly increased quantities. They occur in all mucous membranes, especially in those which are rich in mucous glands (nose, mouth, throat, air-passages). Their course is acute or chronic. The transformations of the mucous membranes themselves and of the mucous glands are slight ; the latter appear only for the most part larger, and their excretory duct is dilated.

A strikingly large production of mucus is found also with a simultaneous serous, purulent, and croupous inflammation. Then the mucous glands are sometimes not only very wide, but their orifices show openings, which perforate the croupous exudation.

e. As types of CROUPOUS EXUDATION are to be regarded those cases of croup of the air-passages in children and adults, and perhaps some cases of croupous inflammation of the lungs. In these cases, primary vascular changes, at least in the dead body, are for the most part moderately developed. The chief circumstance is the quick origin of the firm croup-membrane, consisting of transformed epithelium and pus-corpuscles. Many cases of croupous inflammation of other mucous membranes referred to this class are fibrinous inflammations.

CROUP simply expresses the formation of a croupous membrane upon the mucous membrane of the larynx, and for the most part also on that of the trachea; PSEUDO-CROUP simply a congestive hyperæmia running its course with like symptoms, or simply catarrhal inflammation of the same parts. The French employ another nomenclature ; they call true croup only the first mentioned affection, with simultaneous exudation upon the pharyngeal mucous membrane : pseudo-croup that affection without pharyngeal croup. Croupous inflammations occur sometimes primarily (especially laryngeal croup); sometimes secondarily, *e.g.*, laryngeal croup in scarlet fever measles, small-pox, typhoid fever.

f. PURULENT FORMS of inflammation appear purest, with slight vascular

changes, in secondary inflammations, where the irritant passes with the blood into the organs, as in pyæmia. In other cases, besides acute suppuration, there are often found other phenomena of inflammation : thus marked hyperæmia in inflammations of connective tissue, subcutaneous and intermuscular, of the connective tissue between the intestines and beneath the peritoneum, as in perinephritis, pericystitis, periproctitis, perityphlitis, perichondritis laryngea, peri- or retro-pharyngitis, in the first stage of pneumonia. Also in the periosteum, and in the endostium supporting the marrow, and bearing abundant fat-cells. Very great suppuration occurs also in SEROUS MEMBRANES, in synovial membranes of the joints, especially with high degree of vascular change.

In mucous membranes purulent forms occur sometimes acute, with for the most part marked hyperæmia, as PURULENT CATARRHS ; sometimes chronic and with slight vascular changes, as PURULENT BLENNORRHŒA. In acute inflammations of the mucous membranes (stomatitis, gastritis, colitis, urethritis, inflammations of the ducts of many glands, etc.), sero-purulent or pure purulent exudation is mixed with the substance of the affected mucous membrane ; in the epithelial covering, if composed of many laminæ, there are found at first perhaps increased formation and separation of epithelium, further on pus-cells, which pass through the epithelium into the free surface, and beneath which the epithelial cells themselves often are normal or only moderately enlarged. The tissue itself of the mucous membrane is sometimes only hyperæmic ; sometimes simultaneously also infiltrated with serum, and penetrated by scanty or abundant pus-corpuscles ; in both cases swollen. The mucous glands herein for the most part take no, or only a slight part ; sometimes they show the same process, or stand out, on account of the accumulation of their contents, as small pearl-like nodules (e.g., in *stomatis vesicularis*). Also in the external adventitious connective tissue of mucous membranes there occur perityphlitis, periproctitis, peribronchitis, etc. In the SKIN all these processes are modified by the firm, unyielding, horny layer which lies over the stratum of Malpighi, analogous to the epithelium of mucous membranes. Catarrhal processes are on this account impossible, at least so long as the horny layer remains. If the latter is in any way destroyed, these processes go on in the same manner as in inflammations of mucous membranes : e.g., in acute eczema. Circumscribed suppuration is best observed in the pustules of small-pox, which have the same character, also, in the mucous membranes of the mouth and œsophagus.

The term CATARRH is intelligible only by the conception of the ancients, that in "cold," liquid flows from out of the ventricles of the brain through the ethmoid bone and nose, or is distilled from them, and thus the brain is purified of injurious substances. SCHNEIDER (*De catarrhis*, 1661) first demonstrated anatomically the falsity of this theory.

In PARENCHYMATOUS GLANDULAR ORGANS purulent inflammations sometimes affect the epithelial or other cells of the acini, sometimes the interacinous connective tissue and its vessels are the sources of the pus-corpuscles. In still other cases both conditions at the same time, or transitions of suppuration from one part to another, occur. In the first-mentioned case the gland-cells either remain, as in many suppurations of the renal tubuli, where pus-corpuscles pass out singly or in casts. Or, they are destroyed with the suppuration, which further affects the interstitial tissue, and sometimes gives rise to abscesses. Suppurations of this kind are

oftenest observed in the puerperal mamma, in the testicle, more rarely in the kidneys, salivary glands, lymph-glands, etc. In the LUNGS, suppurative inflammations occur within the alveoli as well as in the interalveolar, interlobular, peribronchial, etc., tissues: they are distinguished as free and interstitial.

In catarrhal pneumonia the epithelia of the pulmonary vesicles swell, their nuclei increase greatly in numbers, then the cells separate and fall into the cavity of the alveoli (RANVIER, *Nouv. dict.*, etc., 1870, XIII., p. 675). According to BUHL (l. c.), pus-corpuscles have their origin in the smallest bronchi, and by inspiration pass into the alveoli.

g. The ULCERATIVE FORM of inflammation passes in various ways into the degenerative forms of inflammation. It affects especially the membranous tissues. Their destruction may follow suppuration or precede it. Ulceration takes place sometimes in consequence of suppuration in the connective tissue of the membrane, sometimes in consequence of preceding fatty metamorphosis of the epithelium and of the connective-tissue corpuscles, of the albuminous infiltration, and of the cell-growth between the connective tissue fibres, which metamorphosis is or is not at the same time accompanied with suppuration. The former occurs in most common ulcers of the skin and mucous membranes; the latter forms most of the falsely-termed diphtheritic inflammations of the intestinal mucous membrane, as in dysentery, cholera; secondarily in small-pox, puerperal fever, etc. In the term ULCER there is implied not only loss of substance, but also new-formation, with destruction of a part of the new-formed material. Owing to the part played by the vessels and suppuration, cohesion is finally destroyed, and there results a breach of the skin or mucous membrane.

The doctrine of ULCERS belongs for the most part to special surgery, where helcology, in the hands of ASTRUC, BELL, RUST, and others, has attained to great perfection. A rational classification of ulcers has hitherto been impossible. They are commonly classified: according to their character into stationary, atonic or torpid, also into corroding and sloughing ulcers, in opposition to healthy ulcers; according to the cause: into local, *i.e.*, dependent upon a local disease, or idiopathic, catarrhal, varicose, diphtheritic (or aphthous), puerperal, simply and constitutionally syphilitic, scorbutic, dysenteric, typhous, tuberculous (and scrofulous), carcinomatous ulcers—to which many refer those designated as lupous, gouty, warty (MARJOLIN), etc.; according to complications: into inflammatory, hyperæmic, anæmic, hæmorrhagic, œdematous, gangrenous ulcers. On some mucous membranes there occurs still a peculiar form of ulcer: follicular ulcers, which have their origin in ulceration of the solitary follicles.

As ulcers, also, are often regarded those disturbances of continuity, in which usually there occurs no continuous production of pus: *e.g.*, typhous and tuberculous ulcers of the intestine, as well as the round ulcer of the stomach. These ulcers are, as a whole, not dependent upon suppuration of the affected membranes, but upon necrosis, in consequence of complete interruption of the circulation; the formation of pus takes place only exceptionally in the ulcer already formed.

In the bones, striated muscles, brain, and liver, suppuration precedes (in abscesses) in many cases degeneration and destruction of tissues; granulations, pus, and ichor appear only when the cavities are pre-formed.

The swellings of the solitary follicles and lymph-glands, as well as of the spleen, frequently occurring in catarrh of mucous membranes from the transition of exudative to the productive forms of inflammation; the swelling is dependent upon increase of the nuclei and cells of the gland juice.

3. PRODUCTIVE INFLAMMATIONS in the narrower sense, which lead to new-formation of PERMANENT TISSUE.

To this class belong, first of all, most subacute and chronic inflammations of SEROUS MEMBRANES, in which vascular connective tissue is generated, which further on lead to general clouding and thickening of the serous membrane, or to tendinous spots, or to the formation of tufts, or to the growing together of both laminæ of the serous membrane, by short or long vascular masses of connective tissue. Similar conditions are found in the joints.

MEYER (*Ann. d. Char.*, XI., p. 1) has directed attention to the importance of adhesive pleuritis, with respect to the resorption of the pleural exudation.

Also to this class belong most chronic inflammations, which affect especially interstitial glandular tissue, and chiefly PARENCHYMATOUS ORGANS; circulatory changes are slight, the vessels of the new connective tissue are at least not excessively filled with blood. Examples are afforded in many interstitial fibrous inflammations (indurations or cirrhoses), of the mammary glands, liver, lungs, testicles, inflammatory thickening of the uterus and its vaginal portion, thickening of the valves of the heart, total or partial sclerosis of the brain; in a word, those of the connective tissue of every part.

In mucous membranes, new-formations of the different layers occur in consequence of chronic inflammations. This sometimes affects all the layers, as in many forms of chronic gastritis (*scirrhus ventriculi*), enteritis, etc., with consecutive contraction of the cavity and diminished contractility, etc. Sometimes only single layers are hypertrophied. The most important is that in the muscular coat of the intestinal canal and urinary bladder above the narrower portion (œsophagus at the cardiac extremity, stomach at the pylorus, urinary bladder in strictures of the urethra, etc.). The mucous membrane itself, as well as the submucous tissue, becomes thicker through increase of their connective tissue and vessels, sometimes also through hypertrophy of the glands. This takes place in inclosed parts, thus giving rise to polypi, in which sometimes the glands, sometimes the connective tissue, sometimes the vessels preponderate. Also papillary new-formations appear, *e.g.*, in chronic cystitis as tufted hypertrophy of the mucous membrane, in inflammation of the vagina as granulations, on the skin of the genitals as condylomata. Chronic periostitis terminates with the deposition of layers of bone, with the formation of prominent osteophytes; chronic inflammations of the medullary membrane of the bones, with fibrous thickening of it and transformation of the connective tissue into osseous tissue. The healing of bone, wounds and cicatrization of wounds of the skin take place only through productive inflammation.

4. DEGENERATIVE FORMS OF INFLAMMATION.

Most parenchymatous inflammations are simply degenerative. Thus, acute and many chronic inflammations of the liver and kidneys, where vascular changes and free exudation are almost entirely wanting: the nutritive fluid entering the cells of the liver, Malpighian capsules and urinary tubuli, which probably is also changed qualitatively, swells them up, and finally the cells are destroyed through albuminous infiltration with or without fatty metamorphosis. In inflamed adipose tissue the fat-cells exhibit serous accumulations, sometimes also a peculiar increase of the nuclei.

Inflammations characterized as DIPHTHERITIS mostly begin with intense hyperæmia, but besides they behave in a very different manner. In diphthe-

ritis of the throat and of the great air-passages there is found on parts of
the epithelium a croupous or croupo-purulent membrane, under which the
mucous membrane, and also for the most part the subjacent tissues, are
interrupted by hæmorrhages and infiltrated by pus.   The loss of epithelium
and the infiltration last-mentioned are, with respect to their extent, de-
pendent upon the superficial or deeper destruction of tissues.   In diphthe-
ritis, falsely so-called, of the intestinal canal, primary (dysentery) as well
as secondary (in cholera, typhus, small-pox, etc.), in that of the uterus, etc.,
there is found on the surface a similar but thinner layer of exudation,
which is made up of purulent mucus, epithelial cells infiltrated with albu-
minous matter, and which have undergone fatty metamorphosis, and the
uppermost infiltrated layer of the mucous membrane ; the connective tissue
corpuscles of the mucous membrane, also of the submucous tissue, in part
become fatty, in part containing abundant pus-corpuscles, which likewise
have suffered fatty transformation, and an abundant fibrino-albuminous
exudation.

Gangrenous may be distinguished from PHAGEDÆNIC inflammations, in
which the parts are destroyed layer by layer and extending peripherically,
after they have previously undergone purulent infiltration.   They are found
in the skin, connective tissue, lungs, etc.

GANGRENE is, in these inflammations, DEPENDENT sometimes upon absolute
stasis of the blood in a large portion of tissue; sometimes upon contact of
pus with putrefying materials ; sometimes upon the fact that the inflamma-
tions themselves has been induced by gangrenous ichor, poisons, contagions ;
sometimes upon paralysis of the inflamed parts ; often upon the fact that
the periphery of the parts has been destroyed by pus.   (*Vide infra*.)

CHEESY INFLAMMATIONS are those in which, usually in a chronic manner,
the for the most part purulent or purulo-fibrinous exudation, or desquamated
epithelium, have, in consequence of the anæmia, lost so much liquid that
there results a dry, gray, or grayish-yellow mass, firmly imbedded in the tis-
sues.   They are observed most frequently in the lungs, rarely in the lym-
phatic glands, bones, brain, etc.

Cheesy pneumonia, according to BUHL (*Lungenentz*, u. s. w., 1872, p. 68), proceeds
from neither catarrhal nor croupous, but only from true desquamative pneumonia.
The latter is characterized by an embryonal increase of connective tissue in the
inter-alveolar tissue, and by an abundant new-formation of cells and nuclei in the
adventitia of the smallest arterial branches, which in different parts forms nodules or
only diffuse swellings.   B. includes in this class also the white pneumonia of the
new-born, which the Author holds to be of syphilitic nature.   (*Arch. d. Heilk.*, 1863,
p. 356.)

TUBERCULOUS INFLAMMATIONS are distinguished either by deposits of an
almost purely fibrinous exudation upon the free surface of serous sacs, of
the alveoli of the lungs, etc., in which there is a constant and more or less
abundant nuclear and cell-formation : thus are they rather cheesy inflam-
mations.   Or, with the phenomena of inflammation, they lead only to great
nuclear and cell-formation, and for the most part to the formation of dis-
tinct miliary or more diffuse tubercle.   Indeed the names in use, of menin-
gitis, epididymitis, pleuritis, etc., TUBERCULOSA point to this connection
between inflammation and the formation of tubercle.   The nuclei and cells,
as well as the fibrin-exudation, very soon suffer cheesy metamorphosis,
whilst the exudation, as well as the new-formed nuclei and cells and the
included pre-existing parts, assume a molecular state, whereby membranes
are destroyed as ulcers, and cavities form in parenchymata, or suffer calca-

reous or atheromatous degeneration. Inflammations of this kind appear very often in people affected by general tuberculosis, especially in the lungs, on serous membranes, and in the mucous membranes of the urinary and sexual apparatuses, in the testicle, etc. (See Tuberculosis.)

5. SPECIFIC INFLAMMATIONS.

They are those which are the results of wholly specific causes, the nature of which, however, is for the most part entirely unknown, and which are characterized chiefly by the nature of the process, as well as by their local-ization, and finally by the peculiar, and likewise, for the most part, specific participation of the whole organism.

A part of the processes to be referred to this class may, with equal justice, be included among the new-formations; as tuberculosis and scrofulosis, typhoid fever, leucocythaemia, lupus, syphiloma, cancer in some cases. Others also belong in part to that list, but are most of them considered here. This holds good, especially of the new-formations in glanders and farcy. Here, upon the local ulcer, there follows affec-tions of an inflammatory nature in the lymphatic vessels and glands. Later there follow cutaneous eruptions, nodular growths and ulcers in the subcutaneous con-nective tissue, in the bone-membranes and in the bones, in the lungs and testicles, and in other internal organs.

III. CLASSIFICATION OF INFLAMMATIONS WITH RESPECT TO THEIR CHAR-ACTER.

Until the present time inflammations have been divided into STHENIC and ASTHENIC, as well as into active and passive. With strong STHENIC inflammations should be denoted the possibility of a favorable termina-tion in strong development of the phenomena. A favorable termination is possible in proportion to the nutrition of the inflamed part. If, in a strong man, and in a part well nourished, the local phenomena of inflam-mation and also fever are present in high degree, the inflammation is then called sthenic. In these cases also the fibrin of the blood is considerably increased; as in acute rheumatism, pneumonia, pleuritis, facial erysipelas, and, too, in traumatic inflammations. Inflammations are said to be HYPER-STHENIC when the local transformation of tissue is so considerable that the part is destroyed by gangrene, by suppuration.

ASTHENIC, torpid, or adynamic inflammations affect parts poorly nour-ished and disposed to degenerations. They arise from slight irritations. Chronic inflammations belong for the most part to this class. In the ætio-logical categories are the metastatic and hypostatic, as well as many inflam-mations of paralyzed parts; in the anatomically divisible forms the diphthe-ritic and the degenerative.

III. GENERAL DISTURBANCES OF NUTRITION.

Normal nutrition consists in morphological and chemical processes. The former until now have been little known, since they have provisionally been almost inaccessible to our means of investigation; the latter, on the other hand, have been more exactly studied, at least with respect to indi-vidual organs, e.g., the muscles.

DISORDERED NUTRITION, so far as it concerns new-formations, is still little known chemically; so much the more has attention been turned to

histological changes. In retrograde changes attention has until now been turned more in both directions.

The nutrition of the elements of the body may be changed in three ways:

1. If the NUTRITION IS INCREASED, the part takes up surplus material, the growth is increased: PROGRESSIVE METAMORPHOSIS; and either in the direction of the old tissue, HYPERTROPHY, HYPERPLASIA: or in a foreign direction, HETEROPLASIA, NEOPLASIA.

2. If THE NUTRITION IS INCOMPLETE, retrogression is increased; the normal form and function are more or less lost: RETROGRADE METAMORPHOSIS, INVOLUTION.

3. If THE NUTRITION IS WHOLLY INTERRUPTED: NECROSIS, GANGRENE.

The different disturbances of nutrition occur sometimes singly, sometimes two or more together, sometimes combined with various disturbances of the circulation, and with inflammation.

1. IMPERFECT NUTRITION, RETROGRADE METAMORPHOSIS.
(ATROPHY, INFILTRATION, AND DEGENERATION.)

(The general literature of the subject is found in writings on general pathology and pathological anatomy. Special literature, *vide infra*.)

THE VARIOUS RETROGRADE METAMORPHOSES HAVE IN COMMON, A DECREASE IN VARIOUS DEGREES OF THE NUTRITION AND FUNCTION OF THE AFFECTED PARTS. In this respect, however, the elements undergoing atrophy tissue behave differently.

a. THEY MERELY DECREASE IN SIZE, their elements diminish in volume, their chemical elements are not changed, only diminished—QUANTITATIVE, SIMPLE, PURE ATROPHY. This simple atrophy, the becoming smaller, falling away of the elements, is yet to be distinguished from NUMERICAL DECREASE OF THE ELEMENTS, wherein a part of them is wholly and forever destroyed (necrobiotic atrophy). In a given case, both forms of atrophy may occur, and, besides these, degenerations often accompany one or another.

b. Into the tissue A FOREIGN SUBSTANCE FROM WITHOUT, from the blood, is DEPOSITED, infiltrated (chalk, pigment, fat), which is followed either by a loss of special function, or at the same time by a change of form, or finally also by a complete destruction of the tissue—INFILTRATION.

c. The tissues are transformed INTO OTHER SHAPES AND MATERIAL, whereby they are for the most part softened and made absorbable: thus albumen into fat, mucus, etc.,—QUALITATIVE ATROPHY, DEGENERATION.

The above classification is not a strict one.

The TRANSFORMATION OF ONE TISSUE INTO ANOTHER, physiologically of a lower grade, but otherwise equal to the normal tissue, is usually not to be regarded as atrophy or degeneration, but clinically is to be ranked with it. Thus, most frequently connective or adipose tissues occupy the place of muscle, nerve, and glandular tissues of all kinds. The opposite condition is found in transformation of common connective tissue into fatty or cytogenic tissue, the fatty marrow of the medullary cavity of bone into lymphoid medulla, etc.

Certain forms of atrophy, which affect whole parts of the body or the whole organism, have formerly, and partly at the present time, been designated by special names. Thus simple emaciation, MACIES, EMACIATIO, MARCOR to express wasting of the fat, is distinguished from decrease in size of the muscles, TABES. Others call tabes a wasting dependent upon affections of the nerves. CONSUMPTION, PHTHISIS, CON-

SUMPTIO were formerly applied to atrophy after ulceration and febrile processes : now they are applied for the most part only to atrophy appearing in the course of chronic pulmonary tuberculosis. HECTIC is applied to emaciation through loss of the fluids, *e.g.*, diarrhœas, hæmorrhages. MARASMUS signifies rather the continuous low condition of nutrition, as it is found in bad nourishment, or normally in old age. CACHEXIA is commonly applied to the state of lasting slight nutrition of younger persons. But these expressions are now often used indiscriminately for atrophy of the whole body, etc., which is acquired by sickness.

Before our knowledge of histological changes, atrophies were divided into indurations and softenings. To INDURATIONS were referred also a number of processes, which consist in hypertrophies or new-formations, especially of connective tissue. Just as ambiguous is the expression SOFTENING. This, like induration, likewise occurs not infrequently under circumstances where no atrophy can be assumed. All œdematous parts are softer, etc. So, *e.g.*, in general emaciation there is a kind of softening of the fat tissue, but which in reality represents a transformation of it into ordinary mucous tissue ; in inflammations, etc., there frequently appears a transformation of the common connective tissue into the same tissue. At other times there arises a softening in consequence of digestion, *e.g.*, softening of the stomach. Softening of the bones may have various causes : in a formation physiologically analogous to that of the medullary cavity, whereby the hard circumference becomes thinner with age, the medullary cavity wider, and cavities are found in the bone, which are filled with granulation or fat cells ; in an enormous new-formation of vessels ; in a resorption of the lime salts (halisteretic form of malacia).

THE CONSEQUENCES OF ATROPHIES

are partly local, partly general in character.

The LOCAL INFLUENCE of atrophies consists for the most part in a diminished, often wholly arrested function of the part affected. Therefore, besides being dependent upon the kind and degree of the atrophy, it is especially dependent upon the importance of the parts.

This influence is so much the greater if the atrophies affect parts which, in the intra-uterine state, are wholly or in part undeveloped. In this event, all CONGENITAL DEFECTS and FISSURES have their origin. These are beyond the limits of our consideration. But in the extra-fœtal state also, and before the completion of growth, proportionately greater consequences follow from the same causes than after complete development: especially in the osseous system. Thus arise local arrests of growth in the length of bones in young persons in consequence of diseases of the intercartilaginous lamella on the epiphyses, etc. (especially suppuration of it and premature ossification in osteo myelitis, caries, and necrosis in the extremities ; resection of joints inclusive of the intercartilaginous layer) ; shortening of the cranial bones, pelvic bones, etc., after previous suppurative or ossifying inflammation of them : the various cranial and pelvic deformities.

The local influence of atrophies, therefore, if we except normal retrogressions of the organism (thymus gland, etc.—puerperal uterus), is always unfavorable with respect to pre-existent tissues. It is favorable, on the other hand, with respect to exudations (pus) and most new-formations, especially those chiefly cellular (tubercle, cancer) : these are thereby diminished in size or may even wholly disappear.

The GENERAL INFLUENCE of atrophies depends upon their kind, grade, and extent, upon the dignity of the organ affected, upon the possibility of reproduction of the destroyed tissues, or of a compensation of their functions. In this connection nothing general can be stated.

Atrophies occur sometimes ALONE, sometimes with one or another DISTURBANCE OF THE CIRCULATION, or INFLAMMATION, or other forms of NUTRITIVE DISTURBANCE. The relation of retrograde metamorphoses to circulatory disturbances varies. Many atrophies are results of certain disturbances

of the circulation: thus simple atrophy and fatty metamorphosis are results of anæmia; pigment metamorphosis a consequence of hyperæmia and hæmorrhage. Or, atrophies are the conditions of disturbances of the circulation: thus lardaceous metamorphosis is followed regularly by anæmia, etc. Or, atrophies are followed by manifold processes.

Thus, in ARTHRITIS DEFORMANS (*malum senile*) there appears at first an atrophy of the articular cartilage; further on, in consequence of the abnormal pressure, etc., inflammation of the synovial membrane and subjacent bone, thickening and increase in size of the former, hypertrophy of the bone, etc. All this is so much the more prominent in the lower extremities, where the mechanical conditions of pressure are most often present and most effective. Still more complicated are the conditions in RACHITIS: the new-formation of cells, which determines the growth of bone in its length as well as thickness, and the formation of the medullary space take place here too quickly or at least to too great an extent and too irregularly, whilst the formation of true bone substance does not go on with equal pace, giving rise thereby to bending. incomplete or complete fractures of the bones, swellings of the articular extremities, etc.

THE CAUSES OF ATROPHIES

lie generally in the fact, either that the tissue-elements do not grow at all or not to sufficient extent, or that their retrogression is more active than their growth.

Atrophies are usually distinguished as ACTIVE and PASSIVE.

The causes of PASSIVE ATROPHIES are:

1. PRESSURE, which may affect an entire part or only its vessels or nerves, is exerted from without or from within, or has its source in degenerations and new-formations. Examples are found in all parts of the body, in external and internal organs. The small feet of the Chinese women, the deformed skulls of many races of people, are effects of this cause. The most striking are the atrophies of bony parts: of the vertebral column by aneurisms; of the vault of the cranium by the Pacchionian bodies; of the articular extremities by abnormal unilateral or uniform pressure, as in long standing or sitting, especially during the period of growth, in luxations and contractures. This form of atrophy is often seen in the skin over varicose veins; in the liver it arises from pressure of contracting connective tissue, etc.

Pressure is the cause of the disappearance of the vessels on the articular surfaces during development, to which pressure they are exposed by use of the joints (TOYNBEE, *Philos. Transact.*, 1841, I., p. 159). If in childhood the various joints are by use exposed to pressure, these vessels recede, and in the adult are found only in the margin of the articular cartilage. (Under various diseased conditions the vessels are formed anew). Also in the explanation of a number of acquired deformities of the joints, abnormal pressure plays an important part. Such anomalous differences of pressure cause an irregular growth of the articular extremities: since where the pressure is abnormally strong, growth is less, where it is diminished, growth is promoted. If the level of ossification sinks somewhat on one side, and rises on the other, the joint becomes oblique.

2. WANT OF NOURISHMENT chiefly, diminished supply of nutritive material. This is either general or local. In the former case the cause may reside without the body (poverty, hunger), or in disorders of the body itself (stenosis of the higher organs of digestion, refusal of food in insanity, etc., general anæmia from different causes). Sometimes a quantitative, sometimes a qualitative diminution of nourishment is present: with respect to the latter a deficiency of lime especially appears to be injurious. Examples of

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locally diminished supply of nutriment are furnished in all forms of anæmias, especially those dependent upon chronic arteritis; venous hyperæmia, since here an insufficient amount of blood flows into the parts; hæmorrhage and dropsy, in so far as they cause pressure upon parts and anæmia.

CHOSSAT showed that if young growing hens are fed for months with washed feed and distilled water, the bones become thin, soft and fragile. According to WEGENER (*Virch. Arch.*, 1872, LV., p. 11), under the simultaneous influence of feeding with phosphorus and deprivation of inorganic substances, *e.g.*, chalk, the mode of growth of the bones suffers a change which corresponds with rachitis in man.

3. DIGESTIVE DISORDERS act in a similar manner (most febrile diseases; many acute and chronic diseases of the stomach and intestinal canal, liver, and pancreas; many diseases of the brain, heart, lungs); also disturbances with respect to resorption (numerous diseases of the heart and lungs connected with venous hyperæmia of the abdominal organs; many diseases of the liver, stomach, and small intestines, and of the mesenteric glands).

4. EXHAUSTING EVACUATIONS (hæmorrhages, excessive secretions and excretions, *e.g.*, excessive lactation, diabetes, albuminuria, great exudations and ulcerations).

5. CONCUSSIONS (see Calcification).

The causes of ACTIVE ATROPHIES are:

1. LESSENED FUNCTION and diminished local irritation: thus bones, muscles, and nerves undergo atrophy when they are not used. In consequence of insufficient use for years, whole extremities not infrequently are atrophied (APLASIA OF INACTIVITY), especially the lower extremities after chronic inflammation of the joints, after caries in children, the fingers of adults in severe *arthritis deformans;* the extremities of bones in stumps after amputation, those which diminish in pseudarthrosis; likewise the lower jaw, after loss of the teeth; the orbits decrease in size after loss of the eyeballs, the cotyloid cavity after unreduced luxation of the hip-joint. In like manner is the inactive portion of the intestine atrophied in artificial anus. Likewise, the testicles grow smaller after an abstinence for years from coition, especially in the later years of life and after previous activity.

If, in consequence of the changed condition of the intermediate lamina of the joint a part of the articular cartilage never comes in contact with the opposite cartilage, the cartilage becomes atrophied: it becomes fibrous, its cells fatty, and the tissue is finally entirely lost (HENKE). Consult VOLKMANN, in PITHA-BILLROTH'S *Hdb. d. Chir.*, 1872, II. B., p. 694.

BONNER and TEISSIER have shown how great the changes may be, which occur in stiff and motionless joints which perform no function. The synovia becomes scanty and disappears; the capsule shrivels; the synovial membrane, through whose arrangement the motion of the joint is only rendered possible, is shortened and finally in part or wholly obliterated. Finally, synechiæ arise between the articular surfaces, even bony anchylosis. Concerning hydrarthrosis of stiff joints, consult VOLKMANN (*Berl. klin. Wschr.*, 1870, Nr. 30–31).

2. EXCESSIVE USE of parts: progressive muscular atrophy after severe straining of the muscles, fatty degeneration of the heart after prolonged and increased activity of it, atrophy of the brain after great fatigue of the mind, atrophy of the testicles after prolonged onanism, emphysema of the lung after habitual crying, etc.

3. Many substances used in the arts or as MEDICAMENTS cause atrophy (lead,—iodine, mercury, phosphorus, alkalies, ergot).

4. Poisons of INFECTIOUS DISEASES (small-pox, diphtheritis, syphilis, etc.) are followed by various metamorphoses directly, or by inflammation.

5. INFLAMMATIONS not infrequently cause atrophies (see p. 272).

6. HIGH FEVER of short duration, or fever continuing for a longer time (see Hectic fever). Fever acts by deficient nourishment, increased consumption of the parts, perhaps also in a peculiar manner (heat of fever): the weight of the body decreases, the urea of the urine is generally increased.

7. The INFLUENCE OF THE NERVES upon disorders of nutrition is in general frequently demonstrable. The nerves act perhaps in part directly: trophic nerves (sudden blanching of the hair, gelatinization of granulations from fright, etc.); in part through the vaso-motor nerves (e.g., section of the sympathetic); in part through the nerves of sensation (thereby unnoticed influence of external injurious irritants); in part through disorder of function (e.g., atrophy of paralyzed members); through loss of appetite, sleeplessness, etc. Most disorders of nutrition, dependent upon the nerves, seem to occur through the vaso-motor nerves. From paralysis of these there arises congestive hyperæmia with increased temperature, which mostly disappears again after quick healing of the nerve-affection, at other times, however, is followed by congestive hyperæmia with retarded circulation, decrease of temperature, and by nutritive disturbances of various kinds (simple consumption, fatty metamorphosis, etc.).

EXPERIMENTAL INVESTIGATIONS have furnished numerous proofs of these views.

As regards the experimental sections of nerves with consecutive atrophy of the parts supplied, the parts indicated in the chapters on disturbances of the circulation (p. 175), on inflammation (p. 244), on gangrene, are to be consulted, besides the known works of MAGENDIE, SCHIFF, and MEISSNER. According to OBOLENSKY (Med. Ctrlbl., 1867, No. 32), section of the spermatic nerve with removal of a piece of it, induces fatty degeneration of the peripheric portion, and, in consequence of the destroyed innervation, in spite of the integrity of the vessels, the same degeneration of the epithelium of the glandular tubes of the testicles, as well as of the epididymis. Thereby the glands are atrophied, and not the interstitial tissue which sometimes is transformed into fat-tissue. LANDOIS and EULENBERG observed in frogs, rabbits, and dogs, after section of the sciatic nerve, great disturbances of nutrition, even gangrene of the foot. Simple section of the great nerve trunks of a member or organ leaves, moreover, the communication not yet completely destroyed, because possibly the nerve-fibres presiding over the vegetative processes follow peculiar courses different from those of the chief trunks. The skin of frogs with destroyed brain and spinal cord always becomes gradually smoother, dry, and discolored; it feels like parchment and stiff (GOLTZ, etc.).—MANTEGAZZA (Giorn. veneto di sc. Med., 3 t. b., 1867) observed, after section of the sciatic, changes also in the connective tissue, periosteum, bones, and lymphatic glands.

After experimental nerve-section, various changes of the muscles have been found. MANTEGAZZA found them smaller, their nuclei and the connective tissue, increased; VULPIAN observed besides an increase of the fat-cells, likewise ERB and lately BIZZOZERO and GOLGI (Oestr. med. Jahrb., 1873, p. 125). The latter observed some muscles in rabbits, 11 months after the section, almost entirely transformed into fatty tissue.

CLINICALLY, and, to a less extent, by pathologico-anatomical observations, a number of atrophies have been demonstrated, which are the consequences of the interrupted influence of vaso-motor, or trophic nerves. The same occur in many of the common cerebral and spinal paralyses, but, above all, in those of the peripheric nerves. In old HEMIPLEGIAS the epidermis is often dry, rough, and scaly, the nails curled, fissured, and brittle; the extremities become thin, especially with simultaneous contrac-

tures. In spinal paralysis all these symptoms are for the most part still more strongly pronounced, so that there frequently result BED-SORE, or gangrene from pressure. This is the most striking and constant in PERIPHERAL PARALYSES. In paralysis of the facial nerve the paralyzed half of the face is more faded and thinner than the normal half; not only the fat, etc., but also the muscles are atrophied. In paralysis, *e.g.*, after section of one or more nerves of an extremity, the skin of the affected parts is cooler (even to many degrees), and bluish-red, and the muscles are atrophied, etc.

MITCHELL, MOREHOUSE, and KEEN (*Gunshot Wounds and other Injuries of Nerves*, 1864) communicate interesting cases of traumatic lesions of nerves and their influence upon nutrition. Consult also SECCHI, *Die durch Nervenverletzungen bedingten Functionsstörungen und trophischen Hautveränderungen*, Bresl. Diss., 1869.

According to NOTHNAGEL (*Arch. f. Psych. u. Nervenkrkh.*, II., 1 H., p. 29) atrophy in parts which are the seat of a neuralgia, depends upon the simultaneous participation of the vaso-motor nerves. In two cases of sciatica, the extremity became pale with the appearance of pain, and felt cold; there was also a subjective feeling of cold, at the same time a feeling as though the part were dead, insensibility, and irritation. The sensibility was also objectively lowered, so that light touches were not at all felt, strong pinching only slightly.

Alopecia senilis coincides with the region of the frontal nerve (O. SIMON).

[Consult : MITCHELL, *Injuries of Nerves*, Phila., 1872.]

To this class also belong many forms of disease rarely occurring, but which by their symptoms, extent, etc., are highly characteristic and very evident to the senses, TROPHO-NEUROSES: many deformities, *atrophia lateralis cruciata*, unilateral atrophy of the face or of an extremity, glosso-pharyngeo-labial paralysis, muscular atrophy, essential infantile paralysis. In these cases the change resides, differently, sometimes in the sympathetic, sometimes in the anterior ganglion cells of the spinal cord, sometimes in determined parts of the medulla oblongata.

[*Vide* paper by Editor, *On Spinal Paralysis*, Trans. N. Y. Acad. of Med. 1874.]

In a series of deformities, with the absence of certain parts of the spinal cord and their nerves, there are also wanting the corresponding voluntary muscles, whilst bones, cartilage, vessels, and skin are normally developed. A rare but striking kind of atrophy exists as CROSSED LATERAL ATROPHY (*atrophia lateralis cruciata*), *i.e.*, atrophy of half of the cerebrum in atrophy of the opposite half of the cerebellum, spinal cord, nerves, muscles, and bones. HEMIATROPHIA FACIALIS consists in a circumscribed total, fixed or progressive atrophy of the skin (or mucous membrane , muscles and bones (even the teeth), with complete integrity of the remainder of the body, and with normal motility and sensibility of the atrophied parts : *e.g.*, atrophy of one cheek, or of one half of the whole head and face, sometimes at the same time with that of the tongue and lower jaw; or, the atrophy affects an extremity (observations of CH. BELL, HIMLY, LOBSTEIN, ROMBERG, STILLING, VIRCHOW, BERGSON, BÄRWINKLE, SEELIGMÜLLER, BRUNNER, EMMINGHAUS, and others [*D. Arch. f. klin. Med.*, 1872, XI., p. 96]). According to BÄRWINKLE, in such cases the affected ganglion is diseased; according to BRUNNER, it depends upon a permanent state of irritation of the cervical sympathetic. In a man 35 years old, otherwise healthy, I saw a case perhaps belonging in this connection, where there was complete wasting of the greatest part of the right inferior maxilla after previous falling of the teeth, and without phenomena of inflammation, suppuration, and gangrene.

In PROGRESSIVE MUSCULAR ATROPHY the cause of the wasting of the muscles likewise resides in the nervous system : according to CRUVEILHIER, SAPPEY, RECKLINGHAUSEN, and others, in the anterior roots of the spinal nerves ; according to SCHNEEVOGHT, REMAK, JACCOUD, and others, in the sympathetic ; according to VALENTINER, VIRCHOW, FROMMANN, FRIEDREICH, and others, in the spinal cord. In ATROPHIA MUSCULORUM LIPOMATOSA, BARTH (*Arch. d. Heilk.*, 1871, XII., p. 121) found an atrophy in the anterior and lateral columns of the spinal cord. In essential paralysis of children, CHARCOT, JOFFROY, VULPIAN, RECKLINGHAUSEN,

BARTH, found degenerations in the anterior horns, antero-lateral columns, and anterior roots of the spinal cord. According to EULENBERG (*Berl. klin. Wschr.*, 1872, Nr. 2) the centres of nutrition of muscles lie in the cells of the anterior horns and extend outward through the anterior roots.

[Consult HAMMOND, *A Treatise on Diseases of the Nervous System.* 6th Ed. N. Y., 1875, p. 449 *et seq.*—ED.]

The above view, according to which atrophy in the nervous system is primary, that at the periphery secondary, has many opponents. The latter assume a directly opposite relation. Many observations support this view. Thus, according to VULPIAN (*Acad. des Sc. Paris*, 26 Febr., 1872), after amputation of the limbs there is a shortening of the diameter of the corresponding half of the spinal cord, especially of the posterior columns and posterior horns, dependent upon simple atrophy. Section of the larger nerves of an extremity is, according to V., followed by the same consequences.

Not infrequently, in special cases, MANY CAUSES of atrophy are present at the same time. In children (*pædatrophia*) atrophy not infrequently appears without other disorders of the body than slight intestinal catarrhs, whilst at other times the most extensive changes are found in the lungs, intestinal canal, and lymphatic glands. Among the former cases there are many which follow from typhoid fever, where, under increasing atrophy of high grade, death appears, and no farther causes are shown by autopsy.

In old people, an atrophy of all tissues occurs normally and slowly : so-called *marasmus senilis.* But a somewhat similar condition, with febrile movement, sometimes occurs in an acute manner : so-called *morbus climacterius.*

A. SIMPLE, OR PURE (QUANTITATIVE) ATROPHY.

(ATROPHIC HARDENING, SCLEROSIS, INDURATION, OBSOLESCENCE, CORNIFICATION, COLLAPSE.—CHEESY DEGENERATION, TUBERCULARIZATION.)

CANSTATT, Art. "*Atrophie*" in Wagner's *Handw. d. Phys.*, 1842, I., p. 27.—ECKER, *Arch. f. Phys. Heilk.*, 1843, II.—VIRCHOW, *Würzb. Verh.*, I., p. 85; II., p. 72.—BUHL, *Ztschr. f. rat. Med.*, 1856, VIII., p. 1.—FÖRSTER, *Virch. Arch.*, 1857, XII., p. 197.

SIMPLE OR PURE ATROPHY is characterized by a decrease at first of the fluid, later of the formed elements of tissues, without simultaneous essential chemical changes. Thereby the affected tissues or organs become smaller, firmer, dryer, but retain their essential texture ; they, for the most part, become poorer in blood, rarely richer in blood, because of the growing smaller of the remaining parts of the tissue ; they suffer in their functional capacity.

Simple atrophy frequently occurs, and affects normal as well as new-formed tissues.

The CAUSES of simple atrophy are, in the main, decrease of nutritive material (hunger, excessive loss of fluids, as especially in diabetes, deficiency of bloodvessels, diseases of the vessels), in consequence of which there is a deficient new-growth (so-called APLASIA), as in senile atrophies. Simple atrophy has been observed in the testicle, in consequence of over-exercise of function. These atrophies arise also in consequence of diminished performance of function : thus, in the bones, joints, nerves, genitals, from various causes. More rarely, simple atrophy depends upon an increased retrograde formation, which occurs most strikingly through long-continued pressure upon tissues (atrophy of all tissues, especially also of the bones by tumors and aneurisms, by intentional external pressure, *e.g.*, upon tumors, callus, etc. ; Atrophy of the kidneys in hydronephrosis, atrophy, so-called

red or cyanotic, of the liver in congestion of the hepatic veins, biliary in accumulations of bile, etc.). The causes of simple atrophy of many new-formations are partly these, partly those which consist in a peculiar disposition of the whole organism (see Scrofulosis).

(Consult Inanition, Diabetes, Ischæmia, etc.)
Of especial interest with respect to the course of fibres in the brain and spinal cord is the degeneration of the spinal cord, first demonstrated by TÜRCK (*Ztschr. d. Ges. d. Wien. Aerzte*, 1850, I. H.; *Wien. acad. Sitz.-Ber.*, 1851, p. 288. See also BARTH, *Arch. d. Heilk.*, 1869, X., p. 433.). Degeneration proceeds finally to the complete disappearance of the medullary sheath. It is a result of the arrested function of the affected parts, begins some weeks after the diseases acting as causes, and is after some months completely developed. In primary diseases of the thalami optici, corpora striata, etc., certain bundles of the pons and of the medulla oblongata are atrophied, the posterior parts of the lateral columns of the spinal cord on the opposite side, etc.
[Consult BOUCHARD, *Secondary Degenerations of the Spinal Cord.* Transl. from the French by E. R. Hun, M.D., Albany, 1869.—ED.]

SIMPLE ATROPHY OF NORMAL TISSUES occurs physiologically : at all ages in the hair, in the upper layers of the skin, and of the mucous membranes with laminated pavement epithelium ; in the fœtal state in some vessels (umbilical vessels, *ductus Botalli*, etc.), in the Wolffian bodies, etc. ; during the first years of life in the thymus gland, in the milk-teeth (*dentes decidui*), in the vessels of the synovial membranes, etc. ; at certain periods of life, especially in old age, in almost all tissues, from the fiftieth year in the genitals, especially the mammary glands and ovaries.

As a cause of SECOND DENTITION, beginning in the seventh year of life, there has been demonstrated an obliteration of the branch of the dental artery : thereby the roots of the deciduous teeth disappear and the crowns become loose and fall off. An ossification of the tooth-pulp appears to precede the falling out of the teeth of old people ; the new-formed bone-substance is like the dentine, nevertheless is less uniform and contains also radiate bone-cavities (NASMYTH).

PATHOLOGICALLY, simple atrophy is present in various tissues as emaciation, and as premature marasmus of age, after severe acute and chronic diseases (typhoid fever, etc.,—pulmonary phthisis, diabetes, etc.). Sometimes it occurs locally from various causes (especially pressure from without, or through internal forces : most distinctly in the skin over large tumors—disappearance of the supplying nutritive or functional vessels, interstitial connective tissue growth). Many metamorphoses of mucous surfaces into membranous forms also belong to this category.

Mechanical forces, according to MENDELSOHN, are also the causes of pulmonary emphysema. During over exertion of the body, playing of wind instruments, attacks of coughing, etc., the glottis is narrowed and lower portion of the thorax is contracted through action of the abdominal muscles. The air, which can only in part escape, or not at all, through the glottis, is thus compressed into the upper lobes of the lungs, whose elastic tissue become gradually relaxed, and this is followed by a permanent distention of the alveoli. According to ISAAKSSOHN (*Virch. Arch.*, 1871, LIII., p. 466), pulmonary emphysema depends upon a peculiar wasting of the vessels, connected with thrombosis.
MENZEL (*Arch. f. klin. Chir.*, 1871, XII., p. 990) further observed experimentally the joint-affection arising from continued rest of the joints, which had already been observed by J. CLOQUET (*Dict. de Méd.*, 1821, VI.), TEISSIER (*Gaz. méd. de Par.*, 1841, p. 609 u. 625), BONNET (*Tr. d. mal. d. artic.*, 1855), and VOLKMANN (*Berl. kl. Wschr.*, 1870, No. 33 ff.). He inclosed the joints in plaster and examined them after 11–68 days. The immovability was never dependent upon the synovial membrane or ligaments, but particularly upon changes in the cartilage.

The synovial membrane was always greatly swollen and reddened. The cartilages were fawn-colored and dull. They showed microscopically, fibrous or ligamentous destruction of the basis substance, and proliferation of cartilage-cells.

In children, the epiglottis is often indented on the sides, partly turned over with its borders somewhat curled, and projects with its free posterior borders very far backward. According to RIEGEL, this form of epiglottis frequently occurs in tuberculous adults and represents a deficient development only—a permanent condition of an earlier form belonging to childhood (*Berl. klin. Wschr.*, 1872, No. 20 et 21).

Simple atrophy affects cells, basis-substance, fibres of all kinds. In particular: epithelium of every kind; gland-cells, especially of the liver, kidneys, mammary glands, testicles, lymphatic glands, spleen; connective-tissue corpuscles; fat-cells (upon the atrophy of which common emaciation is dependent); of the basis substances, those of connective tissue and bones; of fibres, those of striated and smooth muscles, nerve-fibres.

The MICROSCOPIC PROCESSES are not yet entirely known. Common cells (epithelium, gland-cells) become smaller, even like nuclei, or laminated, sometimes clearer, sometimes more granular, with increased resistance to reagents. In fat-cells, instead of simple large fat-drops, there are seen many medium or numerous small fat-drops, surrounded by a serous liquid; finally the fat-cells again become connective-tissue corpuscles; their connective tissue becomes for the most part more abundant. Muscle-fibres become smaller, lose their transverse striation, not infrequently also the longitudinal striæ become softer and more fragile; they are sometimes pale, sometimes contain the ordinary pigment and inter-connective tissue in greater quantity, as well as often numerous nuclei. Nerve-fibres likewise become smaller and poorer especially in medulla, or lose it altogether: this is seen with especial clearness in gray degeneration of the posterior columns, as well as in secondary atrophy of the spinal cord. The connective tissue, capillaries and gland-membranes become denser, more fibrous, with increased resistance to reagents; the connective-tissue corpuscles become smaller, nuclear. In the lungs, atrophy of the tissues leads to dilatation of the alveoli and to the final disappearance of the tissue between two alveoli, with the formation of a communication between them.

In atrophied fat-tissue and in disappearing bone-tissue, in the latter physiologically, processes of growth accompany the atrophy: atrophic growth of fat-tissue, and the multinuclear giant cells of bone. (See New-formations.)

In PAVEMENT EPITHELIUM, atrophy is observed macroscopically and microscopically with especial distinctness in cicatrices of various kinds, also in syphilitic infiltrations (so-called plaques) of the mucous membranes of the mouth and soft palate.

In GLAND-CELLS, simple atrophy is most distinct in high grades of congestive hyperæmia (*e.g.*, of the liver), in bloodvessels, which have suffered extensive fatty degeneration, and in the neighborhood of new-formations. The highest degree of this atrophy, *i.e.*, an entire absence of the liver-cells, is furnished also by the red substance of the liver, in acute yellow atrophy of that organ (ZENKER, *D. Arch. f. klin. Med.*, 1872, X., p. 166).

Concerning ATROPHY OF FAT-TISSUE, consult the investigations of FLEMMING (*Arch. f. Micr. Anat.*, 1870, VII., p. 32). Besides the common retrograde metamorphosis, F. observed that sometimes the fat-cells may again lose their membrane: they are finally represented by membraneless, nuclear heaps of fine fat-globules. FLEMMING (*Ib.*, 1871, VII., p. 328) found, besides serous atrophy of the fat-cells (the usual form of their atrophy), another very frequent and perhaps constant form, which he calls ATROPHIC GROWTH. It consists in this, that in some of the atrophic fat-cells, instead of the old nucleus, many nuclei appear, sometimes so many that the

whole space between the fat and cell-capsule is filled by them; in others, the fat is as if pressed by the mass of surrounding nuclei or small cells; finally, in many the fat has entirely disappeared and is supplanted by an accumulation of denser young cells equal in size to the full fat-cell. The offspring of the fat-cell for the most part become migrating cells, in part also fixed connective tissue cells. The same forms are furnished by fat-tissue in artificially induced inflammation.

FLEMMING (*Virch. Arch.*, 1872, LVI., p. 146) describes also a peculiar atrophy of the capillary meshes in fat-tissue : after the filled fat-cells have disappeared by suppuration, etc., the meshes grow smaller until diminutive spaces are left.

RUGE (*Virch. Arch.*, XLIX., p. 237) found, by comparative measurements of amputation preparations, that an atrophy also appeared in bones through inactivity, and that the bone was atrophied as with age, and by intercellular resorption (contrary to expansion in young bone).

According to NEUMANN (*Wien. acad. Sitzgsber.*, 1869 ; *Wien. Med. Z'g.*, 1869, No. 3), hair-follicles and connective tissue shrink in the senile changes of the skin of man and allow of the formation of wrinkles; in like manner, the epidermis, rete Malpighii and sweat-glands shrivel. The elasticity of the skin diminishes. Dilatation of the vessels in the skin of old people is, according to many, dependent upon a rarefaction of the connective tissue.

Many forms of simple atrophy occur IN THE HAIR: *calvities*, baldness from natural causes, as in old people, in consequence of an atrophy of the hair-follicles; *defluvium capillorum*, falling out of the hair in consequence of febrile and constitutional diseases (especially typhoid fever, constitutional syphilis); *alopecia*, falling out of the hair from local causes and in limited parts, and through inflammation of the skin or hair-follicles (erysipelas, eczema, etc.), through vegetable parasites (*herpes tonsurans*, etc.), through pressure of exudations and tumors, through interrupted nervous influence. WILLAN calls the latter form *porrigo decalvans*, CAZENAVE *vitiligo*, BÄRENSPRUNG *area Celsi*. The anatomical changes are the same as in the atrophy of age (RINDFLEISCH. *Arch. f. Dermatol. u. Syph.*, 1869, I., p. 483). (Consult BÄRENSPRUNG, *Ann. d. Char.*, 1857, VIII., 3. H. p. 59.)

BAMBERGER and RECKLINGHAUSEN (*Wien. Med. Presse*, 1869, No. 27 et 28) found in two cases of progressive muscular atrophy a diminution of the muscular fibres. Fatty degeneration of them and development of fatty tissue between them is shown only locally, manifestly as a secondary or inferior condition. The spinal cord was normal; the anterior roots of the nerves appeared in one case highly atrophied, in the other normal. In the nerves of the muscles, on the other hand, there were found single atrophied nerve-fibres, which had suffered fatty degeneration.

BUHL (*Lungenentz*, u. s. w., 1872) also describes an acute PULMONARY ATROPHY, a consequence of a pneumonia, by him called desquamative. To distinguish it from the otherwise analogous acute atrophy of the liver, the affected parts of the lungs may through atmospheric air experience softening or decomposition.

The consequences of simple atrophy, with respect to the affected tissues and organs, vary greatly with the form and dignity of the latter. Its influence upon the organism is likewise determined in the same manner.

Simple atrophy has many resemblances with COLLAPSE, which for the most part appears very suddenly in extensive hæmorrhages, sweating, evacuations from the stomach and intestine (Asiatic cholera), but depends upon a mere diminution of the watery constituents.

In consequence of continuous lying on the back, collapse appears in the posterior parts of the lungs and succeeding inflammatory infiltration. For the horizontal position causes a diminution of the thoracic space, by forcing toward each other the anterior and posterior walls, as well as by allowing the abdominal contents in this position by gravitation to press against the diaphragm. (BARTELS, *Ber. d. Naturf. Vers.*, 1872, p. 161.)

SIMPLE ATROPHY OF EXUDATIONS AND NEW-FORMATIONS affects cellular and fibrous tissues.

Among the CELL-FORMATIONS, particularly worthy of note, are the cells of pus, those of many lymphomata, those of syphiloma, of tubercle, and

of cancer. If the cells lie in a fluid basis substance, as pus-corpuscles and cancer-cells, this first disappears. Thereupon the cells (or nuclei) lose first a part, then the whole cell-contents : they become thereby smaller, flat, remain rounded or become irregularly angular and more strongly refractive, and are less susceptible to the action of reagents. The cell-nucleus is indistinctly or no longer demonstrable. Finally, the cells or nuclei thus changed are transformed into irregular masses and molecules. At this time a supplementary SOFTENING sometimes reappears, by means of which a RESORPTION occurs, and sometimes a PERFORATION. (If softening does not occur, the purulent cell-masses, rarely those of other character, are ENCAPSULED, i.e., surrounded by a firm connective tissue poor in vessels.)

Simple atrophy is often accompanied simultaneously by a molecular condition of the cellular contents, which is fatty, more rarely calcareous and pigmentary.

Purulent exudations, as well as the affected new-formations, become, in consequence of this atrophy, wholly or in part changed into uniform or punctiform or reticular masses, which are grayish yellow or yellowish, homogeneous, dry, firm, or fragile, or cheesy and bloodless : so-called CHEESY METAMORPHOSIS OR TUBERCULIZATION. They thereby assume a condition so different from their original one, that they were formerly held to be special forms of new-formations (formerly known as raw or crude, now yellow tubercle, carcinoma reticulatum, etc.).

Concerning cheesy metamorphosis, see p. 263. The importance of cheesy metamorphosis of pus-foci, with respect to the origin of miliary tubercle, is considered under the head of Tuberculosis.

TUBERCULIZATION is, therefore, called simple atrophy, because it is almost constant in tubercle, if this exists for some time, and because it was formerly known as tubercle. VIRCHOW first demonstrated its occurrence in other tissues and new-formations.

In FIBROUS NEW-FORMATIONS, atrophy affects the cellular parts as well as the basis substance : the latter becomes indistinctly fibrous or homogeneous, firmer, dryer ; the vessels are partly or wholly destroyed. The entire new-formation becomes smaller, paler, dryer, firmer. This change is found in newly-formed connective tissue of all kinds, in tendons, connective-tissue hypertrophies of the most various organs (granular liver), in cicatricial tissue, where it represents the CICATRICIAL RETRACTION so important in surgery ; further, in connective tissue of tumors, as well of those which are entirely formed of it, as in those where it exists only as stroma. (See Colloid cancer.)

B. DEGENERATIONS, OR QUALITATIVE ATROPHY.

(DEGENERATIONS, METAMORPHOSES, INFILTRATIONS.)

DEGENERATIONS are characterized not merely by change of texture, but by simultaneous chemical changes of the parts. The substances which appear in the tissues, usually IN THE PLACE OF THE NORMAL ALBUMINOUS BODIES, are fat, cholesterin, calcareous salts, mucous and colloid substance and others; pigment. These substances arise either through a metamorphosis of the albuminous bodies (e.g., fat in fatty metamorphosis, mucus), and then resemble the affected physiological substances. Or, they are deposited from out of the blood into the tissues (thus blood-pigment, chalk, fat in fatty infiltration, according to many lardaceous substance) : either because

the blood leaves the vessels in an abnormal manner (*e.g.*, hæmatoidin), or because the blood contains these materials in excessive quantity (*e.g.*, fat in fatty infiltration), or because many tissues abstract the substances in question from the blood with especial energy (*e.g.*, the lardaceous substance).

Another change, besides, is to be mentioned here, which may with almost equal right be included among the inflammations. We treat of it here, since it more or less constantly introduces other degenerations, especially the fatty, and since it frequently occurs without the other phenomena of inflammation. It is the so-called

a. ALBUMINOUS INFILTRATION (or degeneration):

(cloudy swelling, granular albuminous metamorphosis, parenchymatous inflammation).

VIRCHOW, *Arch.*, 1852, IV., p. 261, and in other places.—BUHL, *Ztschr. f. rat. Med.*, 1856, VIII., p. 1. ; *Klinik d. Geburtsk.*, 1861, p. 231.

ALBUMINOUS INFILTRATION consists in a filling of the tissues with molecular albumen. The molecules are exceedingly small, for the most part very pale, rarely dark ; they disappear in acetic acid and potassa ; they are not changed by ether ; are colored red by sugar and sulphuric acid. By this infiltration the tissues become more or less clouded, opaque, and increased in size.

Albuminous infiltration affects cells of all kinds, especially those of the deeper epithelium of the skin, mucous membranes and glands, connective tissue corpuscles, even the basis substance of the latter, smooth and transversely striated muscle-fibres, etc.

MICROSCOPICALLY, epithelial and gland-cells, as well as endothelium, show a less distinct contour ; they lose (in consequence of unknown changes of the cement) at the same time their adhesion one to the other and to the glandular membranes ; their nuclei and nucleoli experience the same change or remain normal (or show segmentation), but for the most part are not visible, or only after the action of acetic acid, because of the dense filling of the cell-contents with albuminous molecules. Thereby the cells become larger and their forms are not infrequently so irregular (in consequence of mutual pressure), that their original forms are no longer recognizable. In still higher grades of degeneration the cells disappear, especially after the addition of water, so that under the microscope almost only free nuclei are visible. The basis substance retains its normal consistence or becomes somewhat softer ; that of cartilage not infrequently shows the same cloudiness as the cells. MUSCLE-FIBRES suffer like changes ; they become broader, softer ; their transverse striation becomes more indistinct.

To the NAKED EYE the organs thus changed afford no character entirely peculiar : for the most part they are slightly enlarged, somewhat softer, or distinctly so, sometimes richly supplied with blood, sometimes poorly supplied, sometimes with normal blood-contents ; transparent parts, like the cornea, vitreous, articular cartilage, are clouded ; the normal lustre of the organs, as of the liver and kidneys, appears dulled.

Cloudy swelling affects sometimes only a part of a tissue or organ, sometimes it affects them throughout their whole extent.

It is especially important in the large glands, *e.g.*, the liver and kidneys, heart and other muscles.

The causes of albuminous swelling are local (many excitants of inflamma-

tion), or general (severe acute diseases, especially those with very high temperature, as typhoid fever, scarlet fever, primary and secondary erysipelas, many forms of puerperal fever, the puerperal infection of the new-born; many cases of pyæmia; severe chronic diseases, especially of the lungs and heart; chronic anæmia; poisoning with phosphorus, arsenic, mineral acids, etc.). The special causes lie for the most part in an increased supply of blood and nutritive material, which is not consumed in sufficient quantity; or in a supply of changed blood.

LIEBERMEISTER (*D. Klin.*, 1859, No. 46, and *Arch. f. klin. Med.*, 1866, I., p. 461 et 543) insists that an excessive elevation of temperature is the cause of the malignant course of a great number of acute febrile diseases. M. SCHULTZE and others have directly demonstrated, with the help of the warming apparatus of the microscope, its deleterious influence upon cellular forms.

Albuminous infiltration runs its course sometimes in a very short time, *i.e.*, within a few hours, sometimes it is developed within a few days, sometimes it becomes a chronic process.

In a woman, thirty years old, previously healthy, who had died six hours after burning (second to third degree) of the whole surface, I found the muscle-fibres of both ventricles of the heart uniformly and greatly clouded by molecular albumen in great quantity, and fat in small quantity; the cortical tubules of the kidneys were uniformly dilated, and filled with molecular albumen in great quantity, and fat in small quantity, and free nuclei. Most internal organs were full of blood.

After albuminous infiltration has lasted a variously long time (hours, days, weeks), the parts either return to their normal condition, if they have not been too greatly changed (healing of the affection in epithelial cells of the mucous membranes, especially in acute catarrh of these cells, parenchymatous inflammation of glands of all kinds, as of the salivary glands, milk-glands, liver, kidneys, lymph-glands, of transversely striated muscles, etc.). Or, they are metamorphosed into a soft mass, which is resorbable. Or, if in the meanwhile life is not destroyed, there appear farther changes, which sometimes are of a retrograde nature: particularly fatty metamorphosis of epithelial and gland-cells, lacerations, *e.g.*, of muscles, softening of basis substances; sometimes of a progressive nature: growth of cellular parts.

The infiltration appearing in consequence of obstruction of the ductus choledochus, etc., as well as acute yellow atrophy of the liver, likewise belongs to this discussion: in the lower grades of the latter, which are not infrequently present in typhoid fever, pyæmia, puerperal fever, etc. (BUHL), the essential disease consists in an albuminous infiltration, and in the presence of large quantities of bile in the liver-cells, without or with slight fatty metamorphosis; in the higher grades, those only known before BUHL, there is a destruction of the cells and resorption of the detritus. FÖRSTER (*Hdb. d. path. Anat.*, 2 Aufl., II., p. 181) describes as chronic parenchymatous hepatitis a process analogous to acute yellow atrophy of the liver, and finally leading to atrophy and granular condition of the liver, without new-formation of connective tissue. Many cases of acute and chronic Bright's disease are wholly analogous to those described affections of the liver. BUHL has recently demonstrated the same infiltration, etc., also in the lungs, where it forms the so-called desquamative or parenchymatous pneumonia (see p. 280–1).

The INFLUENCE of albuminous infiltrations upon the whole organism is determined especially by their degree and extent, as well as by the kind of organ attacked. Perhaps, also, it is dependent upon an overloading of the blood, with products of decomposition of the affected tissues (*e.g.*, muscles).

b. FATTY INFILTRATION AND FATTY METAMORPHOSIS.

REINHARDT, *Traube's Beitr. z. exper. Path.*, 1846, 2 H. ; *Virch. Arch.*, I., p. 20.—VIRCHOW, *Arch.*, 1847, I., p. 94 ; VIII., p. 537 ; X., p. 407 ; XIII., pp. 266 et 288 ; *Würzb. Verh.*, III., p. 349.—ARAN, *Arch. gén.*, 1850.—QUAIN, *Med.-Chir. Transact.*, 1850, XXXIII., p. 121.—HESCHL, *Ztschr. d. Wien. Aerzte.*, 1852.—BARLOW, *On Fatty Degeneration*, 1853.—MICHAELIS, *Prag. Vjhrschr.*, 1853. IV., p. 45.—BUHL (see p. 298).—HOPPE, *Virch. Arch.*, 1855, VIII. p. 127 ; XVII., p. 417.—OPPENHEIMER, *Ueb. progr. fettige Muskelentartung*, 1855.—WUNDT, *Virch. Arch.*, 1856, X., p. 404.—O. WEBER, *Virch. Arch.*, 1858, XIII., p. 74 ; XV., p. 480.—BÖTTCHER, *Virch. Arch.*, 1858, XIII., pp. 227 et 392.—ROKITANSKY, *Ztschr. d. Ges. d. Wien. Aerzte*, 1859.—WALTHER, *Virch. Arch.*, 1861, XX., p. 426.—METTENHEIMER, *Arch. f. wiss. Heilk.*, I.—VOIT, *Z. f. Biol.*, 1869, V., p. 79.

FATTY INFILTRATION, *i.e.*, the filling of tissues with fat which comes from without through the blood, and FATTY METAMORPHOSIS or FATTY DEGENERATION, *i.e.*, the transformation of albuminous into fatty substance in the interior of tissue elements and by their peculiar activity, differ with respect to cause, nature, and consequences, but in all cases are not separable. Finally, fatty infiltration passes in some tissues imperceptibly into hypertrophy and new-formation of fatty tissues.

1. FATTY INFILTRATION is characterized by a deposit from the bloodvessels into the tissues, especially cells, of fat : either because fat is supplied to the tissues in too great quantity (through food rich in fat), or because the fat is not duly consumed by the tissues (*e.g.*, in age, in inactivity, *e.g.*, of the muscles).

Microscopically, fat infiltrated into the tissues has mostly the form of large, sometimes very great drops, which easily coalesce. The cell, in moderate degrees of fatty infiltration, retains its normal vitality and functional activity. In the higher degrees, the cell contains only fat, mostly in form of a single large drop, with the nucleus pressed against the cell-membrane : therewith its functional activity is naturally destroyed. The connective tissue corpuscles are changed in this manner immediately or after preceding division into fat-cells, which then may permanently remain. Gland-cells, *e.g.*, those of the liver, in the highest grades of this infiltration, are like fat-cells, but may probably return to the normal state. Whether gland-cells are finally destroyed in consequence of fatty infiltration alone, has not yet been proven. Clinical experience, *e.g.*, with fatty liver, shows that this is not commonly the case.

Macroscopically, the lower grades of fatty infiltration are not to be recognized. In the higher grades, the affected tissues and organs assume a light yellow color, are more or less enlarged, deprived of blood, and softer. In partial fatty infiltration of organs various forms appear, especially dependent upon the presence of anæmia and hyperæmia in the surrounding tissues.

Physiologically, fatty infiltration is found in its lower grades in the interstitial epithelium during digestion, in liver-cells, subcutaneous, subserous, subsynovial, etc., connective tissue, in the cartilage-cells of man, in the kidneys, etc., of some animals : it is either transient, lasting only a few hours, as in the intestine and liver, or permanent, as in the localities last-mentioned.

Whether all the fat infiltrated into the liver-cells is supplied by the portal vein, as appears to be proven with respect to the physiologically fatty liver of mammals (GLUGE, KÖLLIKER), is doubtful, since TSCHERINOFF has demonstrated that the use of sugar as food increased the fatty contents of the liver still more than the more abundant use of fat.

As a diseased condition, fatty infiltration (of the epithelium of the small intestine) occurs in liver-cells, epithelium of the gall-bladder; partly also in renal epithelium, connective-tissue corpuscles, etc.; partly from unknown causes, partly in consequence of abnormal accumulation of fat in the blood. Of especial practical interest is fatty liver in its higher grades. It is found in alcohol-drinkers, in general fatty degeneration, sometimes in chronic pulmonary tuberculosis, in acute phosphorus poisoning, and in acute trichinosis. In paralysis, fatty infiltration is met with in the muscles.

Various theories exist respecting the causes of fatty liver. It is either dependent upon a too great quantity of fat in the blood, as in habitual eating and drinking. Or, it has its foundation in an imperfect oxidation of the fat taken as food, as in many pulmonary tuberculoses. According to many, there exists in such cases a direct metastasis of fat: the fat is resorbed, *e.g.*, in *panniculus adiposus*, in one part and deposited into another, the liver (RINDFLEISCH, *Lehrb.*, 1871, p. 50). According to O. NAUMANN (*Arch. f. Anat. Phys.*, u. s. w., 1871, p. 41), the common cases of pathologically fatty liver are not to be considered as simple deposits of fat from out of the blood, but the fat is produced by a peculiar activity of the liver, or retains at least those peculiarities by which it is distinguished from other fats, *e.g.*, easier oxidizability. Pathological fatty infiltrations of the liver have the same signification for the diseased organism as the physiological infiltration for the healthy organism: they assist nature, being easily assimilable in the diseased body, by supplying necessary fat for its continued preservation.

2. FATTY METAMORPHOSIS.

FATTY METAMORPHOSIS consists in a TRANSFORMATION OF PROTEIN SUBSTANCES into fat-drops, which as to size are very small or molecular, and which for the most part do not coalesce, because they still have an albuminous envelope. In the higher grades this increases to such an extent, that finally the tissue or portion of tissue loses its structure; thereupon they lose this cohesion, and for the most part become resorbed. The function of tissues which have suffered fatty degeneration is, with the degree of degeneration, diminished or altogether suspended.

Fat has its origin probably in processes in which the nitrogen of albuminous bodies disappears in the form of soluble compounds (urea, etc.), and fat remains as a second (insoluble) product of decomposition of albuminous substance.

The PROOFS OF THE FORMATION OF FAT FROM ALBUMINOUS BODIES are partly physiological, partly chemical, partly pathological. With reference to the latter, acute phosphorus poisoning is of especial weight. As the above assumption was probably made from earlier microscopical investigations, it has now also been sustained chemically by accurate experiments by feeding.

The PHYSIOLOGICAL proofs are:

1. Fattening during feeding with sugar and flesh free from fat (PETTENKOFER, VOIT, and others);—the dog excreted during feeding with pure flesh all of its nitrogen as urea, but retains a portion of the carbon, and, as it follows from researches on respiration, as fat (PETTENKOFER and VOIT).

2. The formation of wax (chemically very similar to fat) by bees during feeding with albumen and sugar (FISCHER).

3. During feeding with flesh, without fat, the milk (of the dog) is relatively and absolutely most abundant in fat. It increases in quantity as its fatty contents (SUBOTIN, KEMMERICH);—the food of cows contains not so much fat as the milk, but the decomposed albumen provides for the production of the fat of the milk (VOIT, KÜHN, FLEISCHER).

4. During the development of the ova of the *Limnæus stagnalis* the fat increases three to four fold (BURDACH).

5. During feeding of *muscida vomitoria* with pure calf's blood, the animals acquired seven to eleven times greater quantity of fat than the blood contained (F. HOFF-MANN).

Further proofs are furnished by Fermentation :

6. During the formation of adipocire in parts of muscles (without diminution of volume), fixed fatty acids (QUAIN, VIRCHOW) are found after certain chemical investigations (WETHERILL).

7. During the transition of casein into cheese, albumen decreases, fat increases (researches on cheese by BLONDEAU; contradicted but not disproved by BRASSIER).

8. During standing of milk its fatty constituents increase (HOPPE, SUBOTIN, and others).

Direct CHEMICAL proofs are :

9. The formation of the lower members of series of fatty acids by oxidation and putrefaction of albuminous bodies, as well as during their decomposition by liquefying alkalies.

10. The formation of leucin (belonging to the fatty acids) during putrefaction and digestion of albuminous bodies.

A PATHOLOGICAL proof is :

11. The fatty transformation of tissues in various diseases, *e.g.*, acute phosphorus poisoning, during increase of excretion of urea (PANUM).

JOS. BAUER (*Ztschr. f. Biol.*, 1871, VII., p. 63) starved a dog twelve days (the excretion of nitrogen, decomposition of albumen, had reached a constant, permanent minimum, eight grm. daily), and then poisoned it with small doses of phosphorus. The excretion of nitrogen then until death increased with tolerably uniformity almost threefold (23.9 grm. daily), and the increased excretion of nitrogen corresponded quite nearly with the increasing severity of the phenomena of poisoning. O. STORCH (*Deutsches Arch.*, II., p. 264) had already made similar investigations with similar results, but the nitrogenous (urea) portions of the urine were determined by LIEBIG'S methods, which, as was discovered later, did not in this case appear to be adequate. BAUER estimated the nitrogen directly by heating with carbonate of soda, besides also the urea according to LIEBIG, and obtained by both methods results which agreed very nearly with those obtained before. Hence it certainly follows : that in acute phosphorus poisoning the consumption of albumen is essentially increased ; and since a dog, after twelve days' starvation, has already consumed the circulation-albumen and lives on the organ-albumen, this increased metamorphosis of albumen must affect the albumen of the tissues. Since, besides, after starvation for so long time, dogs have lost almost all fat perceptible to the naked eye, the fat appearing in the tissues during phosphorus poisoning can have its origin only in the transformed albumen of the organism, or be a product of separation of this albumen deposited into the tissues. Comparative estimates of fat in the muscles and liver of healthy dogs and of dogs poisoned with phosphorus, lead to the conclusion that these tissues contain three times as much fat in dogs poisoned by phosphorus as in healthy animals. Some rudimentary researches on the respiration also make it probable that in phosphorus poisoning the absorption of oxygen is to a large extent (one-half) prevented, so that accumulations of fat in the tissues are not dependent merely upon increased formation, but also upon diminished consumption of it.

TRANSPLANTATIONS furnished a negative result. R. WAGNER observed decrease in weight and increase of fat in the testicles and crystalline lens ; MIDDELDORPF, in his researches with rabbits, found fat only in the cavities ; likewise DONDERS, in his researches with tendon, cornea, and cartilage, only in the cellular parts ; BURDACH, in wood and elder-pith. Pieces of albumen and the lens inclosed in impervious membranes (caoutchouc, collodion) remain unchanged in weight and structure ; upon the pouch there is formed a fatty exudation (BURDACH).

Fatty metamorphosis affects normal tissues and new-formations of almost every kind. It is either primary, or follows albuminous degeneration.

MICROSCOPICALLY, it is quite equally represented in the various parts of tissues. In cells there are observed, mostly at first in the neighborhood of the nucleus, sometimes even within the latter, one or more fatty molecules, which are characterized by their great brightness and dark contour, by not being colored by carmine, by their black color with perosmic acid, and by their resistance to most micro-chemical reagents (ether dissolves them—often only after previous addition of acetic acid or caustic alkalies). The

fat-molecules further increase in quantity, whereby they are sometimes most abundant in the vicinity of the nucleus, sometimes uniformly distributed through the whole cell-contents. The cell itself uniformly enlarges to sometimes more than twice its size, and acquires, if of different shape, a round and globular form. If the cells lie imbedded in a more permanent basis substance, as *e.g.*, the connective-tissue corpuscles, they likewise grow larger, but retain in general their spindle-shaped or stellate form. Finally, the whole cell is filled with fat-drops of equal size, sometimes differing in size, and in close contact with one another; their membrane, so-called, is still present; the nucleus is sometimes there, sometimes it is at least invisible. A granular cell is a body of this kind, consisting entirely of fat-molecules or small fat-drops, surrounded by a true membrane or an external, non-fatty layer of protoplasm. After this cell has existed for a longer or shorter time, the membrane (true or apparent) finally disappears with or without increase of fat-drops: the form is then termed granular mass. After a longer or shorter existence of the latter, the fat-drops, held together by the remaining protoplasmic substance, are dissolved first in the periphery, or the whole granular mass divides into many aggregations of fat-drops, and finally into single fat-drops, which swim in a liquid always alkaline. This mass is called fatty detritus. Fat-molecules are either resorbed, or if resorption is obstructed, there are developed from them crystals of fatty acids (margarin, margaric acid, stearic acid), and cholesterin.

Cholesterin, which in great quantity is easily recognized by the naked eye by its glittering appearance, usually forms very thin rhombic plates overlying one another, the acute angles of which amount to 79° 30'. The tables are rarely almost right-angular (87° 30'), or the angles are more acute (57° 20'). It is wholly insoluble in water; easily soluble in boiling alcohol and in ether, chloroform, ethereal oils and fats, less so in solutions of salts of the biliary acids and in soaps. By a mixture of sulphuric acid 5 parts and water 1 part, cholesterin tables are colored first rusty-brown, then a beautiful purple-red, and finally they liquefy into brown drop-like forms. By the addition of concentrated sulphuric acid and some iodine they become carmine-red, blue, and green. Margaric acid (mixture of palmitic and stearic acids) consists of tufts of very fine curved needles, more rarely of sword-like plates. Margarin (mixture of palmitin and stearin) forms for the most part large, tufted or gland-shaped masses of very fine, straight needles. Stearic as well as palmitic acids consist of elongated, pointed, rhombic single or radiated tables.

Possibly, fat-molecules pass in other ways out of the cells, at least out of those which are contractile.

According to STRICKER (*Sitzgsber. d. Wien. Acad.*, LIII., p. 184) the colostrum corpuscles, *e.g.*, of milk analogous to fat-cells, at a temperature of 40° C., show slow but distinct changes of form. The fat-globules gradually approach the surface from the middle of the corpuscle, then they come upon the surface and are finally expelled. The process of milk-secretion may therefore be so conceived that the colostrum corpuscles, as thrown-off enchyma-cells of the gland or as products of division of these cells, expel by active contractions that which they generate within their own body, without even affecting their own life. SCHWARZ (*Ibid.*, LIV., p. 63) saw not only the fat-globules expelled, but also that the whole protoplasmic portion of the body of the colostrum corpuscle is then resolved to undergo still farther changes of form and place. According to LEIDESDORF-STRICKER (*Molesch. Unters.* X., 1866), the granular cell has still at its periphery a zone of basis substance, which is free from granules, on account of which its outline appears defined; in the granular fat-globule this zone is also studded with granules, hence its surface is uneven and granular. The granular cells from the fragments of tissues, taken from living animals, show on the warm stage of the microscope amœboid movements.

Fatty metamorphosis of the nuclei behaves like that of the cells, of fibrous parts (muscle-fibres—modified cells), and of the different seeming or true basis substances (capillaries, cartilage, cornea, etc.). In the latter fatty metamorphosis for the most part appears only when their cells have become fatty.

Fatty metamorphosis begins in transversely striated muscles usually as albuminous infiltration; following the latter is the appearance of fine fat-drops, mostly in the vicinity of the nuclei of the muscles and in the nuclei themselves, rarely within the fibrillæ: the fat-moleeules are mostly arranged in rows, parallel to the longitudinal striæ of the muscles. They increase in quantity, until finally all the contractile substance has disappeared, and the muscle-fibres consist wholly of long rows of fine or somewhat larger fat-drops, which lead at last to the entire wasting of the muscle. In many cases the process deviates from that described (METTENHEIMER and others).
KRYLOW (*Virch. Arch.*, XLIV., p. 477) determined quantitatively the fat of the muscular structure of the heart in a number of diseases: the per cent. in fresh muscles fluctuated between 1.7 and 4.2.

Fatty metamorphosis can easily be recognized with the naked eye, except in its lowest grades, and where but little extended. The affected tissues and organs have a yellowish-gray or yellowish coloration of the surface externally and in section, which is rarely uniform throughout the whole organ, but oftener appears as spots, streaks, etc. The organ is enlarged to various extents, and is more or less anæmic, according to the extent of the fatty metamorphosis; its consistency is diminished. The latter is especially the case, when, besides the cells, the basis substance also has degenerated into fat (cartilage, bone); or when, besides the tissues thus degenerated, there are present fluid or soft substances, *e.g.*, softened basis substances, as in the intima of the great arteries (atheromatous focus). Fluids, in which a great quantity of cells degenerated into fat are found, have an appearance similar to that of colostrum, milk, or butter.

In rare cases, parts far advanced in fatty degeneration do not appear yellow, but have some other color: thus the jejunum in fatty metamorphosis of its muscle-fibres has a reddish, the villi of the small intestines in fatty infiltration assume a blackish color. (The Author, *Arch. d. Heilk.*, II., p. 455.)

The duration of fatty metamorphosis is sometimes short, so that within a few hours, or within a day or few days, the highest grades of it appear (as in acute phosphorus poisoning, in acute inflammations); sometimes it is longer, lasting weeks, months, and years (as in fibrinous exudation, in many diseases of the glands, etc.).

LEIDESDORF and STRICKER (l. c.), within ONE DAY after wounding the brains of chickens, saw granular cells in the vicinity of the wounded cortical substance. After several days the tissue to about 2 mm. in depth was composed only of granular cells and fibres. An equally quick fatty metamorphosis is to be found in the epithelium of the mouth, etc., and of the skin, *e.g.*, in variolous inflammations of these parts.

The CAUSES of fatty metamorphosis are all disturbances of the circulation and of nutrition. These are either primary, or they occur as results of: marasmus; of age; inactivity of parts affected (especially muscles); arrested nervous influence; pressure by extravasations, exudations, newformations. In all these cases, anæmia is the essential disturbance. Some poisons, especially those which dissolve and destroy the blood-corpuscles (alcohol, ether, chloroform; phosphorus, arsenic and antimony; carbonic oxide; sulphuric, phosphoric, and arsenic acids; strychnine; biliary acids),

—some contagia, as that of small-pox, scarlet fever, puerperal fever—the gangrenous ichors of hospital gangrene are followed by a greater or less degree of fatty metamorphosis. These poisons, etc., probably act by rendering the blood unfit for the nourishment of the affected tissues (in part in consequence of a destruction of the red blood-corpuscles).

In hypertrophic organs and new-formations of every kind, especially those formed largely of cells, fatty metamorphosis is comparatively frequent, probably because there is not at the same time a proportionate new-formation of capillaries, or because the new-formed tissues, from whatever cause, have need of more nutritive material.

PONFICK (*Berl. kl. Wchschr.*, 1873, No. 1 *et.* 2) draws a distinction between a fatty heart where the muscular portion has been previously hypertrophic or (very rarely) atrophic, and one where this portion is normal. In the former only portions of the heart are affected, in the latter the whole heart; localized, and generalized fatty degeneration. The former is found in diseases of the heart, diseases of the aorta, nephritis, etc., in pulmonary diseases; the latter (true fatty metamorphosis) in acute, for the most part infectious diseases, from certain toxic substances (phosphorus, arsenic, etc.). In this consideration belongs also the always chronic, pure or idiopathic fatty heart. It is either plethoric, so-called (senile), dependent upon local insufficiency of the bloodvessels to remove the normal quantity of blood; or anæmic, part phenomenon of a general deficiency of blood in normal vessels.

OEDMANSSON (*Nord. med. Arch.*, I., 4, p. 73) frequently found in the umbilical vessels of syphilitic infants at birth, chiefly in the external portion of the intima, advanced atheromatous process, and in consequence of it, thrombosis of the principal and secondary vessels. The syphilis in such cases was transmitted through the father.

The immediate cause of fatty metamorphosis is still unknown. It may be dependent upon the effect of a too small supply of oxygen, through arrested or destroyed nutrition, whereby the fat, which in the same quantity as normally proceeds from the decomposition of albumen, does not receive enough oxygen for its complete oxidation. Or there may be a greater than normal decomposition of albumen, so that more fat is generated than can be oxidized (VOIT).

Besides through the causes mentioned, cases of general fatty degeneration of almost all organs and tissues have been seen without the discovery of an ætiological factor.

A number of these cases belong probably to acute phosphorus poisoning. After HAUFF (*Württ. Corr.-Bl.*, 1861, No. 34) had first pointed out the frequent coincidence of fatty liver with acute phosphorus poisoning, the same coincidence was experimentally demonstrated by EHRLE, KÖHLER, RENZ (*Tüb. Diss.*, 1861), by LEWIN (*Virch. Arch.*, XXI., p. 506), by MUNK and LEYDEN (*Die ac. Phosphorvergiftung*, 1865). The Author (*Arch. d. Heilk.*, 1862, III., p. 359) found a fatty metamorphosis of nearly all the organs of the body. This condition was confirmed by FRITZ, RANVIER and VERLIAC (*Arch. gén. Jul.*, 1862), also by MANNKOPF (*Wien. med. Wochenschr.*, 1863, No. 26). WEGNER (*Virch. Arch.*, 1872, LV., p. 11) also found fatty degeneration in the peripheric parts of the arterial system as far as the arterioles, least marked in the brain, cartilage, medulla of bones and liver.

EBSTEIN (*Virch. Arch.*, 1872, LV., p. 469) investigated experimentally the changes of the gastric mucous membrane, by introducing phosphorus (and alcohol) into the stomach.

Other cases of fatty metamorphosis of almost all organs occur in child-bed (HECKER, *Mon.-Schr. f. Geburtsk.*, XXIX., p. 321).

BUHL has described a peculiar fatty degeneration of the new-born (HECKER u. BUHL, *Klin. d. Geburtsk.*, 1861, p. 296). FÜRSTENBERG saw similar processes in lambs (*Virch. Arch.*, XXIX., p. 152), ROLOFF in swine (*Ib.*, XXXIII., p. 553), BUHL in colts (HECKER and BUHL, l. c.), VOIT in geese (l. c.).

A fatty metamorphosis entirely like that which occurs pathologically occurs in the normal condition of the organism.

Thus it is with the fatty metamorphosis of gland-cells in behalf of the formation of their secretions, *e.g.*, colostrum and milk, as well as of the

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sebaceous matter ; fatty metamorphosis of many organs as a link in their
development, as of the milk-glands, sebaceous and sweat-glands ; fatty
metamorphosis of the epithelium (*membrana granulosa*) of the Graafian
follicles, by which the yellow layer surrounding the extravasation arises ;
fatty metamorphosis of organic muscle-fibres of the uterus, which begins on
the fifth to eighth day after delivery, and probably leads to the disappear-
ance of the whole muscular apparatus.   Fatty metamorphosis is also physi-
ologically probable in the anterior lobes of the pituitary glands, in the
cortex of the supra-renal glands ; also that of the epithelium of the seminal
ducts in adult manhood, and especially in old age.   Fatty metamorphosis
is always found in some epithelial cells of serous membranes.

According to many, the *decidua reflexa* is destroyed by fatty metamorphosis.   In
the *decidua vera* there is not infrequently found a high grade of fatty metamorphosis
of the cellular elements.
According to JASTROWITZ (*Arch. f. Psych.*, II., p. 389 ; III., p. 162) the inter-
stitial encephalitis of the new-born, described by VIRCHOW (see p. 307), does not
represent a pathological but the normal condition, and is to be regarded as a tran-
sition step from the foetal formation of the brain to that of the developed man.   The
more circumscribed partial form of the transformation is found prominently in those
individuals, who, born before time, are backward in their development, and are
anæmic and cachectic.   According to J., the fifth month of foetal life is the time for
the beginning of this change.   Likewise after birth the number of granular cells
again gradually diminish.   At about the seventh month of life they have entirely
disappeared.   J. holds that the appearance of the granular cells is of essential
importance for the formation of the medulla of nerves.   The occurrence, on the
other hand, of fatty degeneration in foci in the cortex is an abnormal one.

Pathological fatty metamorphosis occurs very often.   It affects tissues of
almost every kind, normal as well as new-formed.

Fatty metamorphosis of CELLS is frequent and varies in importance with
the organ.   It is found especially in the epithelium of mucous membranes,
not infrequently during catarrhs, and constantly in the cutaneous epithelium
in pustular inflammations and ulcers.   Fatty metamorphosis of gland-cells
forms in and of itself, or simultaneously with changes in the vessels and
stroma, a series of the most important glandular diseases.   It occurs in
all glands not infrequently in various grades ; practically, it is of the
greatest importance in the kidneys.

Fatty metamorphosis of the muscles affects both smooth and transversely
striated, normal and hypertrophied muscles, especially also the heart.

Fatty metamorphosis of smooth muscle-fibres is of especial importance in arteries
of every calibre, when it occurs for the most part simultaneously with disease of the
intima.
Fatty metamorphosis of transversely striated muscles affects those of the body and
extremities, especially where their function is slightly or wholly arrested through
disease of the brain, nerves, bones, and joints.   It occurs also as a peculiar, some-
times hereditary process (progressive muscular atrophy).   According to CALLENDER
(*Lancet*, 1867, 1., No 2), fatty degeneration of the diaphragm is not only in itself
important as an independent cause of death, but also as a complication of other
diseases.   Fatty metamorphosis of the heart occurs, especially in the ventricles,
from various causes, as well in the normally large as in hypertrophic hearts, in an
uniform, or regular and finely punctated manner, rarely in the form of large irregu-
lar patches.

Fatty metamorphosis of CONNECTIVE TISSUE affects, for the most part,
only the corpuscles, also rarely the basis substance.   It occurs in all varieties
of it, and in all organs which are made up of it, most frequently in the
intima of arteries ; more rarely in the corium of the skin, mucous mem-

branes, in the neuroglia, etc. ; often in the interior and in the periphery of acute and chronic foci of inflammation, in new-formations. Fatty metamorphosis of the cornea, especially of its corpuscles, is met with under like circumstances, being as well a process of old age: *arcus senilis* or *gerontocon.*

CARTILAGE shows normally a small quantity of fat in its cells. A greater filling of the cells with fat occurs pathologically, also more rarely such a filling of the basis substance, especially in great age, in acute and chronic inflammations, *e.g.*, of articular cartilage, mostly with coexisting affections of the other parts of the articulation.

BONES show a fatty metamorphosis of the bone-cells, of the body as well as of the processes, in various acute and chronic inflammations with suppuration, in new-formations, as well as sometimes in osteomalacia.

Fatty metamorphosis of NERVE-TISSUE affects all parts of the nervous system, and is primarily and secondarily important (from pressure, hæmorrhages, inflammations, and in new-formations).

The granular cells met with in various acute and chronic inflammations, with softening of the central parts of the nervous system, are probably fatty connective-tissue corpuscles of the neuroglia (or pus-corpuscles) ; perhaps, also, in very small part, fatty ganglion cells. Fatty metamorphosis of nerve-fibres of the brain (and of those of the spinal cord) is still questionable. Congenital interstitial encephalitis, or myelitis, shows a constant fatty metamorphosis of the neuroglia-cells ; often, also, of the vessels (VIRCHOW, *Arch.*, XXXVIII., p. 129 ; XLIV., p. 472), according to GOLGI (*Virch. Arch.*, LI., p. 568), of the endothelium of the lymph-channels. (See p. 306.)—HUGUENIN (*Arch. f. Psych.*, 1872, III., p. 515) found in a case of cerebral embolism, that all cellular and nuclear elements, which were in the embolic focus, became granular globules, and also the nuclei of the neuroglia, the cells of the capillaries, the cells of the adventitia of the bloodvessels, their muscular nuclei, the cells of the external layer of the perivascular lymph-spaces, the spindle-shaped ganglion cells of the lowermost cortical layer, and those of the gray matter outside of the extra-ventricular part of the corpus callosum. According to MESCHEDE (*Virch. Arch.*, XXXIV., pp. 81, *et* 249 ; *Ib.*, LVI., p. 100), fatty pigmentary degeneration of the ganglion cells of the cerebrum is the most constant pathologico-anatomical change of the brain in paralytic insanity. Consult also MEYNERT, *Ztschr. f. Psych.*, I., p. 386. HOFFMANN, *Nederl. Tijdschr. v. Gen.*, 1868. SCHÜLE, *Allg. Ztschr. f. Psych.*, 1868, XXV., p. 507, but especially L. MEYER, *Arch. f. Psych.*, III., p. 1 *et* p. 242. In the spinal cord a fatty metamorphosis occurs in part as in the brain, in part dependent upon various affections of the brain, which consist in a destruction of brain-substance. It results finally in simple atrophy. (See p. 294.)

In the peripheric nerve-fibres, after section at their peripheric extremities, after destruction of the central parts of the nerves, or separation of the nerve from them, also after destruction of the peripheric distribution of the nerves (*e.g.*, in the n. opticus and acousticus after destruction of the eye and internal ear), in inflammation, gangrene, in the vicinity of tumors, etc., in the spinal cord, within the unchanged sheath (not in the axis cylinder), there are first seen large fat-drops (coagulated medulla with axis cylinder), these fat-drops always increase in quantity and smallness, and are finally resorbed, so that the sheath remains as filamentous, here and there nucleated striæ, with scanty fat-molecules. A fatty metamorphosis of the peripheric extremities of the nerves has been observed only in the Pacinian corpuscles and in the corpuscles of touch (MEISSNER). LANGERHANS (*Virch. Arch.*, 1868, XLIV., p. 413), on the other hand, could never demonstrate a secondary degeneration of the corpuscles of touch in anatomical lesions of high degree in the brain and spinal cord.

Fatty metamorphosis affects all kinds of VESSELS, especially arteries and capillaries, and sometimes all their tunics. The process is sometimes primary, sometimes dependent upon various affections of parenchymata. It is one of the most important diseases of the vessels.

In the CAPILLARIES it affects the nuclei and the tissues immediately adjacent,

more rarely other parts of the membrane.   According to BILLROTH (*Arch. d. Heilk.*, III , p. 47), fatty degeneration of the cerebral capillaries is not an envelopment of them with fat, and not a cause but a result of a disturbance of nutrition of the central nerve-tissue, in many cases perhaps a *post mortem* appearance.   In the ARTERIES it affects the epithelium, the normal as well as the hypertrophic intima, the organic muscle-fibres of the media, more rarely the cells of the adventitia.

Fatty degeneration of the placenta occurs in different ways : that of the peripheric cells of the mature fœtal placenta (normal involution) ; fatty destruction of the cells of the cellular stroma ; fatty degeneration of blood-coagula, etc. (WEDL, SCANZONI, ERCOLANI, FRANKEL, and others).

Concerning fatty metamorphosis of new-formed tissues, see the consideration of these tissues, especially Tubercle and Cancer.

The CONSEQUENCES of fatty metamorphosis for the different tissues consist in a diminished or, in a manifold manner changed, or wholly arrested function.

Fatty metamorphosis of epithelia deprives the affected membranes of their protection, whereby various disturbances arise : on the skin and mucous membranes erosions and ulcerations.   Fatty metamorphosis of gland cells is followed by an arrest of specific function, and thereby by various local or general disturbances (as, *e.g.*, in the kidneys by albuminuria).   In the vessels, through fatty metamorphosis of the endothelium, there occur deposits of fibrin with diseases of the deeper lying parts. Fatty metamorphosis of muscular parts causes loss of contractility to the extent of complete paralysis, which in the heart is especially important, and is the cause of the severest disturbances of the circulation ; that of the *musculi papillares* may be followed by insufficiency of the corresponding valves, that of other parts of the heart by dilatation, formation of fixed thrombi, etc.   Fatty metamorphosis of organic muscle-fibres causes dilatations of cavities to the walls of which they are distributed (also cylindrical and pouched bronchiectases).   Fatty metamorphosis of the nerve-elements is followed by loss of specific functions, etc.

Further injury grows out of a DIMINUTION OF CONSISTENCE : *e.g.*, compression and wasting of articular cartilage with consecutive inflammation of the subjacent bone in *malum senile*, so-called, of the joints ; dilatation of the heart and vessels ; softening of the brain ; lacerations of the heart, vessels, and other membranes, etc.

All these results are so much the more important, when they occur in organs already affected by other changes, as softening of the basis substance (atheromatous ulcers and foci), fatty degeneration of the vessels, thickening of the gland-membranes, etc.

II. MÜLLER (*Würzb. med. Ztschr.*, 1864, V., p. 12) found in the arteries of the brain and choroid of a person dead from Bright's disease, a high degree of fatty degeneration of the endothelium, which had led to a separation of the endothelia, and obstruction of the lumen of the vessels to a great extent.

A COMPLETE WASTING of tissues and organs during fatty degeneration occurs for the most part only in some of their elements (in individual epithelia, gland-cells, muscle-fibres, etc.).   In exudations and new-formations this is beneficial, since these may thereby wholly or in part be again removed from the organism ; often in cellular hypertrophies, especially of the lymph-glands, tonsils, etc., in fibrinous and purulent exudations, for the most part only partially in tubercle and cancer.

JOLLY (STRICKER, *Studien*, etc., 1870, I., p. 38) found in his researches on trau-

matic encephalitis, which, induced mostly in young hens, passed into the various stages of inflammation in from six hours to twenty-one days, that the formation of fatty granular cells is no infallible sign of destruction. Out of a part of the granular mass in the capillaries, within and beneath the adventitia of the finer arteries and veins, there grow ribbon-like and spindle-shaped fibres, which help to introduce the cicatrization of the inflammatory focus. Besides, free granular cells of like form and destiny have their origin in the tissues from the white corpuscles of the blood, and probably from the cells of the neuroglia, and ganglion-cells.

A resorption of fat-molecules from degenerated tissues and a COMPLETE RESTITUTION of the latter is probable only in slight or moderate degrees of the degeneration, and possible when the causative forces have ceased to operate.

The GENERAL CONSEQUENCES of fatty metamorphosis depend upon the kind and extent of the organ attacked, upon the suddenness of its appearance, duration, complications, etc.

In acute fatty degeneration of the new-born, children ordinarily well nourished are mostly born asphyxiated, evacuate, besides diarrhœic liquids, blood by the rectum or vomit it, become icteric after 3–6 days, and often there is generally on the fifth day an uncontrollable hæmorrhage from the navel. Many other organs also exhibit hæmorrhages, external and internal.

Fatty metamorphosis and fatty infiltration are sometimes not to be distinguished from each other, and one not infrequently occurs by the side of the other; e.g., in the cartilages and vessel-walls in old age, in the liver and kidneys in many forms of poisoning.

Likewise, there is a difference between fatty metamorphosis and increase of fat tissue by enlargement and new-formation of fat-cells, the interstitial growth of fat-tissue. The latter for the most part accompanies consecutive atrophy of the limiting parts, especially of the transversely striated muscles in fattening of the body, etc., around atrophic organs, especially the kidneys, etc. But not infrequently both fatty degeneration and new-formation of fat-tissue occur together in certain parts (e.g., in the muscles of the body, during progressive muscular atrophy, in the bones in osteomalacia).

c. PIGMENTARY INFILTRATION, OR PIGMENTARY METAMORPHOSIS.

(Pigmentation, chromatosis, melanosis.)

BRUCH, Unters. zur Kenntn. d. körn. Pigments der Wirbelthiere, 1844.—ZWICKY, De corp. lect. origine atque transform., 1844.—N. GUILLOT, Arch. gén., 1845.—HASSE and KÖLLIKER, Ztschr f. rat. Med., 1846. IV., p. 8; Ztschr. f. wiss. Zool., I., p. 260.—ECKER, Ztschr. f. rat. Med., 1847, VI.—VIRCHOW. Arch., 1847, I., p. 379; II., p. 587; IV., p. 515; VI., p. 259.—SANDERSON, Monthly Journ., Sept. and Dec., 1851.—REMAK, Müller's Arch., 1852, p. 115.—FÖRSTER, Virch Arch., 1857, XII., p. 197.—JAFFÉ, Virch. Arch., 1858, XIII., p. 192.—ZENKER, J.-Ber. d. Ges. f. Natur u. Heilk. in Dresden, 1858, p. 53.—VALENTINER, Günsburg's Ztschr. f. klin. Med., 1859, I., p. 46.—GROHE, Virch. Arch., 1861, XX., p. 306.—HESCHL, Ztschr. d. Wien. Aerzte, VI.; Oestr. Ztschr. f. pract. Heilk., 1862, No. 40, 42, 44.—LANGHANS, Virch. Arch., 1869, XLIX., p. 66.

PIGMENTARY METAMORPHOSIS consists in the appearance of variously colored and variously shaped bodies—HÆMATOIDIN (luteïn) and MELANIN—having their origin in the metamorphosed coloring matter of the blood (hæmatin).

HÆMATOIDIN is diffuse, or granular, or crystalline.

DIFFUSE HÆMATOIDIN causes a more or less uniform yellow or reddish coloration of the tissues affected, and soon passes into one of the following forms GRANULAR HÆMATOIDIN shows, in proportion to its age and according to the organ in which it arises, all shades of color, from a light-yellow to red and black. It is, according to the locality where found, its development, etc., finely or coarsely granular, whereby the granules are sometimes isolated, sometimes grouped in masses of various sizes, round, angular, or pouched. CRYSTALLINE HÆMATOIDIN consists of regularly formed, oblique rhombic columns, which are often almost pure rhomboids. Their size varies from that wherein they are just perceptible to that with a diameter of about 0.1 mm.; in general it also varies slightly in thickness and in breadth. The crystals are strongly refractive and translucent, sometimes even transparent, with a slightly glistening surface. Its color is generally brick-red, but varies with the thickness of the crystals, in part also with the organs. Besides this crystalline form, needles are met with in rare cases, with an orange-yellow or brownish-red color, single, or in radiate or irregularly formed groups. The granules are free or inclosed in cells and flake-like masses, the crystals mostly free.

Granular as well as crystalline hæmatoidin is insoluble in water, alcohol, ether, acetic acid, dilute mineral acids and alkalies. By the hydrate of potash it usually becomes burning red; but it gradually loosens and breaks into red granules, which after a time dissolve. By concentrated mineral acids, especially sulphuric acid, sometimes also nitric acid, the sharp contours of the crystals disappear and there follows a play of colors similar to that observed in the reaction of the coloring matter of the bile; the bodies gradually become brownish-red, green, blue, rose-colored, and finally dissolve into a dirty yellow, leaving behind a finely granular cloud. This reaction does not always appear with the order given and with equal clearness, or sometimes a color is lost.

According to ROBIN, granular hæmatoidin (R.'s hæmatosine) differs also chemically from crystallizable hæmatoidin.

Besides the hæmatoidin the following coloring matters of the blood are worthy of notice; HÆMOGLOBIN, or HÆMATOCRYSTALLIN, or HÆMATOGLOBULIN, the physiological red coloring matter of the blood, which consists of an albumen (globulin?) and a coloring matter, hæmatin; HÆMATIN, which is important especially in combination with muriatic acid, as HÆMIN. PREYER (*Med. Ctrbl.*, 1871, No. 4) found still another kind of blood-crystals, which he calls HÆMATOIN. They are mostly needle-shaped, often bent, arranged in radiate groups or singly, for the most part very sharply pointed. Their size is more considerable than that of all other blood-crystals. They are insoluble in ether, alcohol, water, slightly soluble in caustic potash and dilute acetic acid.

MELANIN is a dark-brown or black, granular or irregularly crystalline substance, probably very rich in carbon, occurring rarely in rhombic plates, very little susceptible to all reagents, the origin of which is probably similar to that of hæmatoidin. It occurs as the known physiological coloring matter in the rete Malpighii of the white and colored races of men, likewise in the eye (within the epithelium as well as the connective tissue cells), in ganglion-cells, in the arachnoid of the spinal cord. It occurs pathologically, especially in gangrene and in many new-formations.

Hæmatoidin has its origin either in a retardation and stagnation of the circulation, or (and most often) in an extravasation of blood. In both cases the coloring matter of the blood remains sometimes within the blood-corpuscles, which then are immediately and entirely transformed into pigment granules. For the most part, however, it leaves these behind and

mixes with the surrounding fluid substances or infiltrates the bounding fixed elements, especially cells of all kinds. It is further transformed from out of this diffuse state into granular or crystalline hæmatoidin. Otherwise the blood-corpuscles remain sometimes within the vessels, and the coloring matter of the blood oozes through their walls. Usually, however, the coloring matter leaves the bloodvessels with the blood-corpuscles : either in consequence of a laceration of the vessels, or, without this, *per diapedesin*.

The coloring matter of the blood, escaped from out of the blood-corpuscles, mixes first with free fluids or with those of the vicinity inclosed in cells. In the former case the blood-serum (œdema in gaugrene, serum in pulmonary œdema), exudations, etc., are colored more or less yellow or brown. The imbibition of the coloring matter of the blood is more distinct in fixed parts. These may be with or without form, physiological or pathological ; sometimes fibrinous coagula, most frequently cells of different kinds, less often fibres and intercellular substances. That hæmatoidin, especially its rhombic form, is found so often in and upon fat-drops, lies in the great mutual adhesion of hæmatoidin and fat, closely related to the coloring matter of bile. (LANGHANS.)

Infiltration of hæmatin into cells is often unequal, since usually of the cell-contents alone, the nucleus rarely alone, shows the coloration. (The same freedom of the nucleus is found also in physiological pigmentation of the external skin, choroid and arachnoid.) The contents of the cell and of the nucleus are very rarely colored at the same time and uniformly. The cell-membrane always remains uncolored ; it shows, by diffusion of the cell-contents, no trace of coloration.

After hæmatin has remained (days and weeks) in the diffuse state, it gradually condenses into small, more distinctly colored granules and masses. Their size varies from that which is first visible, molecules no longer recognizable by their form, to that of a red blood-corpuscle and more. Their form is rarely round, oftener somewhat angular and elongated. Their contours are always very sharp and dark ; their surface is light, bright, and often shining. The color is sometimes yellowish or reddish in various shades, sometimes brownish-red, blackish brown or black. The color of the pigment granules is generally quite constant for individual organs. During this transformation of diffuse into granular pigment, often no change is demonstrable in the elementary parts themselves, which contain pigment ; the cells, *e.g.*, either remain, and for the most part are, probably, capable of function, or they may also suffer fatty degeneration.

Whilst the coloring matter of the blood, escaping from out of the blood-corpuscles, enters upon these changes, the blood-corpuscles themselves have become very pale and smaller. In their border, not infrequently also in the middle of them, there are afterward seen 1–4 and more very small, sharply-defined granules, with a dark contour, light in the centre and colorless, and like fat, which granules are sometimes single, sometimes form a row, sometimes assume a crescentic shape These gradually diminish in number, until only 1–2 of them are seen, bounded by a hardly perceptible membrane. The membrane finally disappears entirely, and only the granules remain, which finally also disappear. The granules, as well as the inclosing membrane, suffer no change in water, dilute acetic acid, and dilute alkalies. Concentrated acetic and mineral acids and alkalies dissolve them completely.

From PREYER's observations (*Virch. Arch.*, XXX., p. 417) on the penetration of foreign bodies into contractile cells, a formation of pigment cells by the taking up of permanent pigment may be assumed.

If the coloring matter of the blood remains within the blood-corpuscles, the latter become smaller, denser, darker, and gradually more resistent to reagents. Thereby they either remain isolated, which seldom happens, or many (5–15) unite into irregular or rounded masses. These masses blend together more and more, and are finally resolved into triplets, or mulberry-like forms, or only into a single, dense granule of pigment broken into fragments by pressure, or finally into the crystals above mentioned. All these forms either occur free, or they are surrounded by a colorless, light, rounded or elongated; or, analogous to pigment masses, lobed boundary similar to a cell-membrane, which, however, possesses none of the peculiarities of a membrane permeable and separable from the cell-contents. Many of these bodies are not at all or hardly to be distinguished from cells containing blood-corpuscles. (See p. 217.)

The above assumption, that the coloring matter of the blood leaves the

blood-corpuscles and is transformed first into diffuse, then into granular and crystalline hæmatoidin, is opposed by the more recent facts obtained by experiment. According to this there first arise cells containing blood-corpuscles, since the contractile cells of the vicinity of the extravasation take up into themselves red blood-corpuscles. The latter are changed chemically and morphologically, and become at first a coarsely granular, or crystalline pigment, which farther on always becomes finely granular and finally diffuse. A part of the pigment-cells become spindle-shaped, others are dissolved, the pigment becomes free, and finally disappears.

LANGHANS made the experiments referred to. He introduced the blood, obtained from a vein or by killing the animal (rabbit and guinea-pigs), in a coagulated state, as quickly as possible under the skin of the same or of another animal, then closed the small wound by suture, and after a certain time killed the animal. In the above mammals the coagulum at first, by loss of serum (which always remains colorless), becomes smaller and firmer ; its fibrin gradually disappears by simple solution (in greater part already in twenty-four hours), and the red globules (the three different kinds) inclosed by the latter remain in the connective-tissue membranes, which are found in the vicinity of the coagulum. The colorless cells in the greatest part of the coagulum shrink, and often the previous formation of vacuoles is destroyed ; only those in the most superficial layers suffer perhaps a similar fate as the cells in the neighborhood. In the latter there results an accumulation of contractile cells, which, from the fourth to the sixth day, take up into themselves the red corpuscles (1–10 and more) by coming in contact with them. The inclosed red-corpuscles are, for a small portion, disk-like and bright, for the greater part spherical and darker ; they are as large as normal, or much smaller. The blood-corpuscles are now transformed into pigment. The chemical changes consist in this, that they at first become darker and most resistant to reagents, but sometimes yellowish to a yellowish red ; still later the color is a reddish yellow, red, or brownish red ; they become more brilliant and have a darker contour. The morphological changes consist in a simultaneous destruction of the disks and globules ; these appear at first irregularly bounded, comparatively large, angular corpuscles, and very fine, angular, intensely colored, and very shining granules. Toward the end of the third week, and still later, there are found in the connective tissues spindle-cells with pigment with the same properties as that found in the contractile cells : the former, according to L., proceed from the latter. Lastly, finely granular pigment is observed always to increase until finally the granules become so fine that they present the appearance of a diffuse pigment infiltration. The cell-substance is then, always with a free nucleus, uniformly colored, and the color is brighter and deeper yellow. Infiltration of cells with yellow diffuse pigment is thus the last stage in the history of pigment, not the first, as has been assumed until now. L. found it always only in the second and third week. The pigmented contractile cells, not transformed into spindle-cells, are finally destroyed by fatty metamorphosis, and the pigment contained in them becomes free. (Many anomalous conditions occur in doves.)

Observations made by ECKER (Z. f. rat. Med., 1847, VI., p. 87), HENLE (Ib., p. 100), KÖLLIKER (Z. f. wiss. Zool., 1849, I., p. 260), the author (Arch. d. Heilk., 1869, X., p. 337), show that cells containing blood-corpuscles occur under the same or similar conditions also in man. This is oftenest seen during pulmonary congestions from insufficiency of the mitral value : the small quantity of air, the peculiar yellow or browish-red color, the increased consistence, weight, etc., of such lungs is dependent upon the accumulations of epithelium containing blood-corpuscles in all stages in the alveoli of the lungs. In a case of insufficiency of the aortic values, with paroxyms, from time to time, of dyspnœa, I found many times in the course of two years that the sputa expectorated contained epithelium like this.

On the other hand, that the coloring matter of the blood escapes out of the blood-corpuscles, at least in extravasations, which quickly thicken through loss of serum, is not yet proven. LANGHANS, in his experiments, never saw the serum and surrounding connective tissues diffusely colored. The contractile cells, makers of the granular pigment, take up the coloring matter of the blood diffused in the serum only after death. In the experiments where L. destroyed the blood-corpuscles by repeated freezing and thawing, and thereafter introduced them under the skin, the diffused coloring matter of the blood was simply resorbed and was transformed neither within nor outside of the cells into granular pigment.

The time within which the varions metamorphoses into hæmatoidin occur probably differs very greatly. The shortest time within which crystals form amounts to only a few days, for the most part from one to two weeks.

I saw in the case of a man 23 years old who had been crushed between two railroad coaches, and had died on the 12th day with symptoms of subacute peritonitis, the whole parietal and visceral peritoneum enclosed by a layer 2 mm. thick of old blood coagula which had come from two ruptures of the liver. In all the layers of the coagula there were found numerous reddish-brown pigment-needles and small rhombic crystals.

The length of time hæmatoidin remains in the body varies. That it finally disappears in most cases is certain. Nothing, however, is known concerning the more immediate processes.

Experience with hæmorrhages of the skin from contusions shows that hæmatoidin disappears quite quickly, whilst the pigment in the cicatrices of chronic ulcers of the thigh not infrequently remains ten years almost unchanged.

Hæmatoidin was for a long time considered identical with bilirubin, and because bilirubin (from bile) like hæmatoidin (from extravasations of blood) separated from its solutions in chloroform always in crystal of the same form and color. But it was afterward demonstrated that hæmatoidin (the coloring matter of the yolk of the egg and corpora lutea) is throughout different from bilirubin of the bile. The orange-red coloring matter of blood-extravasations consists not merely of "hæmatoidin," but also of bilirubin, so that it does not appear improper to call the pigment identical with the coloring matter of the corpora lutea not hæmatoidin, but lutein.

HOLM and STAEDELER (*Journ. f. pract. Chemie*, 1867, C., p. 142) demonstrated that hæmatoidin and bilirubin are entirely distinct. Well-formed crystals of hæmatoidin by reflected light appear beautifully green (like cantharides), those of bilirubin, orange-red. Hæmatoidin dissolves in bisulphide of carbon with a flame-red or, in dilute solutions, with an orange-red color, bilirubin with a golden yellow. The latter enters into combinations in fixed proportions with alkalies, and is soluble in alkalies, the former not; therefore from a solution of the latter in chloroform it may be separated by agitation with caustic alkalies, which is not true of the former. Bilirubin furnishes with nitric containing nitrous acid in alcoholic solution, a beautiful play of colors; green, blue, violet, red, yellow (reaction of biliary matters); hæmatoidin, on the other hand, by nitrous acid is colored light-blue, and then becomes either yellow or colorless. Lutein, according to THUDICHUM (*Med. Ctrlbl.*, 1869, No. 1), is also identical with the yellow coloring-matter of butter, fat, blood-serum, and many plants (flowers, stamens, seeds).

SALKOWSKY (*Hoppe-Seyler, Med.-chem. Unters.*, 3 II., p. 436) found, on the other hand, that hæmatoidin from a strumous cyst had all the peculiarities of bilirubin. He concludes that the hæmatoidin (from the corpora lutea) investigated by HOLM was not pure, or that there are different kinds of hæmatoidin.

Besides bilirubin ($C_{30}H_{18}N_2O_6$) there are found in bile (gall-stones) still other coloring matters, bilifuscin ($C_{32}H_{40}N_2O_7$), biliprasin ($C_{32}H_{22}N_2O_{12}$), and bilihumin, which may be considered as offsprings of bilirubin. Biliverdin ($C_{32}H_{20}N_2O_{10}$?), which has not yet been demonstrated beyond doubt as a natural occurrence, may be artificially produced from bilirubin.

According to PERLS (*Kön. med. Ges.*, Nov., 1866), non-crystalline pigments arising from the coloring matter of the blood become blue by the action of ferrocyanide of potassium and pure muriatic acid (forming Berlin blue), the pigment of the choroid, and probably those derived from fat or the coloring matter of the bile, do not.

The dark-red, reddish-brown, and black pigment molecules, sometimes occurring in the interior of the hepatic cells, probably have their origin in the normal coloring-matter of the bile occurring in the hepatic cells.

While disturbances of the circulation, especially both forms of hyperæ-
mia, thrombosis and hæmorrhage, are known as the causes of the formation
of hæmatoidin, we know only very imperfectly the more immediate causes
of the formation of melanin. This holds true of the physiological pigmen-
tation of the skin, eye, which varies greatly in intensity with the race,
family, etc., and of the muscle-fibres of the heart. This is farther true of
discolorations of the skin dependent upon like histological conditions (pig-
mentation of the rete Malpighii), which almost constantly occur in the linea
alba, the areolæ of the mammæ, etc., during pregnancy, and sometimes in
the face (*chloasma uterinum*) in uterine diseases, and after delivery, etc.,
they mostly disappear again. Similar colorations affect the skin and many
mucous membranes in Addison's disease, or bronzed skin, probably complex
symptoms dependent upon a disease of the abdominal ganglia. In hysteri-
cal persons of both sexes analogous discolorations have been observed, espe-
cially of the skin of the face. Sometimes in those of the female sex there
have been observed the formation of a colored cutaneous secretion (*chromo-
krinia, stearrhœa nigricans*). Finally, there are a number of well-estab-
lished cases, where by excitation of the nervous system (fear, anguish, etc.),
or by severe diseases of the brain, acute or chronic, of high or low grade,
there result local or general dark, even negro-like discoloration of the skin.
(Opposed to this, lighter discolorations of some parts of the skin have been
observed in neuralgia and anæsthesia, permanent or again disappearing with
the causative disease.)

The changes in the color of the skin of many animals, especially the chameleon,
are in the various conditions of the animal (feeling comfortable or angry) dependent
upon the states of contraction of the star-shaped pigment-cells of the skin. They
are thus not analogous to the nervous pigmentation of man.

Hæmatoidin metamorphosis occurs also under PHYSIOLOGICAL conditions.
This is true especially of the formation of the corpora lutea of the ovaries.
Hæmatoidin occurs in many organs so often that it may be considered
almost physiological: thus, in the sheath of the cerebral vessels, in the
epithelium of the choroid plexus.

The blood effused from out of the vessels of the Graafian follicle into its cavity
coagulates, and for a few months is but little changed. On about the fourth month
the coagulum begins to undergo atrophy; its centre shows discolored blood-corpuscles
as well as pigment in diffuse, granular, and crystalline form, beautiful brick or vermil-
ion-red crystals, free or enclosed in cells. Sometimes bodies otherwise colored are
present instead of the corpora lutea : *e.g.*, corpora nigra in consequence of the trans-
formation of the extravasation into black pigment, or corpora albida in slight effu-
sions of blood (as in old women).

Hæmatoidin metamorphosis is often found PATHOLOGICALLY. In and of
itself it is of slight importance, since it does not materially affect the func-
tion of parts, except where the pigment occurs in very great quantity, as
well as in cases occurring only under special circumstances, where the pig-
ment enters the vessels and obstructs the capillaries (melanæmia). It is to
be concluded from the presence of pigment that hyperæmia, and particularly
hæmorrhage of various kinds, have occurred once or repeatedly; thus is to
be inferred from the punctated or striated black coloration of the spleen the
earlier presence of strong hyperæmia, etc., as it occurs in attacks of inter-
mittent fever; from large quantities of pigment in the adventitia of the
small cerebral vessels, cerebral congestions, etc.; but the contrary infer-
ence is not allowable: for in many cases of extravasation of blood the color-

ing matter of the blood is resorbed without undergoing a pigmentary metamorphosis, etc. (See p. 219.) Only where the early stages of the development of this pigment are met with, is its origin from the blood certain.

Pigmentary metamorphosis affects normal tissues of all kinds which are vascular or lie in close proximity to vessels: cells, as epithelium, gland-cells of every kind (also of the spleen and lymph-glands), endothelium; connective tissue of every kind, especially that of the skin, mucous and serous membranes, the adventitia of the vessels, the connective tissue of the lungs, the connective tissue of the glands, especially that of the lymph and milk glands; muscle-fibres, transversely striated and smooth; brain- and nerve-substance.

Pigmentation of the SKIN affects either the rete Malpighii or the corium. Pigment in the rete Malpighii occurs in small degree normally, in higher grades (not regarding the colored races of men whose children are not colored till a few days after birth, as well as of men with congenital or acquired darker complexion) in freckles of summer, in chloasma and in melasma, and Addison's disease. Pigmentation of the corium occurs after hyperæmiæ by warm poultices, mustard-plasters, blisters, etc.; after chronic inflammations, especially in the vicinity of ulcers of the leg of long duration, in dark moles, in very rare cases of true melanosis.

SEROUS MEMBRANES for the most part show a black, usually spotted, rarely uniform pigmentation after inflammations and hæmorrhages. The pigment is usually deposited in the connective-tissue corpuscles. (A peculiar reddish pigmentation, which occurs especially on the external surface of the upper part of the jejunum, has its seat not in the serous membranes, but in the organic muscle-fibres; but the coloring substance is of a fatty nature.) (See p. 304.) The pigment in the sheath of the small cerebral vessels is also of a fatty nature. (STEIN, *Nonn. de pigmento*, etc., Dorpat, 1858.)

MUCOUS MEMBRANES mostly show a black, rarely a brown, and for the most part spotted pigmentation after chronic catarrhs and hæmorrhages, sometimes also in consequence of long retardation of the blood, *e.g.*, in the cavity of the stomach. Pigment is seldom deposited into the epithelium of the mucous membrane or glands, mostly in the tissue of the mucous membrane. The very frequent black coloration of the villi of the small intestine arises not by common pigment, but by one, like fat, soluble in ether. In many cases of this kind no catarrh is present, but probably the fat comes from the blood, which in gastric and other bleedings enters the intestine and here is resorbed by the villi.

Pigmentary metamorphosis in the VESSELS occurs most frequently in the adventitia of the smallest arteries: hæmorrhagic pachymeningitis especially affords beautiful preparations of this kind.

Pigmentary metamorphosis of the remaining tissues and organs has little pathological importance. Concerning pigmentation of the lungs, see p. 64.

In the blood of the NEW-BORN, and in decomposed fœtuses, NEUMANN (*Arch. d. Heilk.*, VIII., p. 170, and IX., p. 40) often found numerous needle-shaped crystals of bilirubin. The formation of crystals was always *post mortem*. All new-born children thus afflicted were affected afterward by *icterus neonatorum*. Crystals were found especially from the second to the seventh day of life, only where the coloring matter of the bile excreted during life was present in solution in the blood. Respiratory disturbances are probably always the immediate causes of crystallization. Infarctions of uric acid are almost constantly found at the same time in the kidneys. In rotten fœtuses the formation of crystals has its foundation probably in a metamorphosis of the coloring matter of the blood into bile-pigment after the death of the fœtus.

VIRCHOW (*Arch.*, XXXVII., p. 212) describes as *ochronosis* a peculiar black coloration of almost all the cartilages and ligaments of the large and small joints of the synovial membranes, cartilages of the respiratory organs, intervertebral ligaments, of the intima of the large arteries, etc., which occurred in a man sixty-seven years old. The coloration of the cartilage varied in various parts, from light gray to black. The microscope revealed brown or yellow granules deposited into the intercellular substance. The color was probably dependent upon a derivation of the coloring matter of the blood. The costal and bronchial cartilages generally show in old people a dark color through deposit of fine pigment molecules. The case cited repeats this condition to a more intense degree.

Pigmentary metamorphosis of new-formed tissues of all kinds, if they are vascular, affects especially new-formed connective tissue, as pseudo-membranes of serous membranes, new-formation of vascular connective tissue upon the inner surface of the dura mater, hypertrophies of connective tissue, cicatricial tissue, tumors, etc. In some cases pigmentation (and extravasation) is more important or observable than the new-formation itself of connective tissue and vessels : *e.g.*, in inter-meningeal apoplexy, in melanotic sarcomata and cancers.

According to NEUMANN (*Arch. d. Heilk.*, 1871, XII., p. 66), melanosis, like fatty degeneration and cheesy transformation, is to be regarded as a peculiar form of retrograde change of the tissues.

Pure pigment tumors or MELANOMATA, *i.e.*, new-formations, which consist of pre-existent connective tissue and pigment in quantities deposited therein. They rarely occur, most frequently in the choroid and iris.

VIRCHOW (*Arch.*, XVI., p. 181) relates a case in which the cerebral and spinal pia mater presented all transitions from scattered and diffuse colorations to tumor-like brown and black nodules, and even showed transitions to sarcoma. ROKITANSKY (*Allg. Wien. Ztg.*, 1861, No. 15) relates a similar case. I found in a case of exquisite melanosis of the skin, and melanotic cancers of various parts, the connective tissue corpuscles of the skin, subcutaneous adipose tissue, peri- and endocardium, etc., as well as the muscle-corpuscles, so strongly filled with pigment, that there was thereby produced only an abnormal coloring of the affected parts, in part larger and smaller black nodules (*Arch d. Heilk*, V., p. 280).

The chapters devoted respectively to other kinds of abnormal coloration, are to be consulted : by substances, which enter the organism from without (p. 64) ; by anæmia, hyperæmia, and hæmorrhage ; by metamorphoses and infiltrations, especially the fatty coloring ; that by bile (see Icterus), etc.

After very long internal use of nitrate of silver there are sometimes to be observed slate-colored or black colorations at first of the nails, then of the remaining parts of the skin, of the albuginea, of the mucous membrane of the mouth and soft-palate, even of the cerebral meninges, of cartilage and bone, of the serous membranes, most mucous membranes, of the membrane of the glands, of the kidneys. They depend upon impregnation by silver in a finely divided state. (Observations by SWEDIAUER, ALBERS, RAYER, WEDEMEYER, FALCK, ROKITANSKY, DELIOUX, and others. GEUNS, *Arch. f. d. Holl. Beitr.*, 1858, I., p. 106.)

PSEUDO-PIGMENTATION, or PSEUDO-MELANOSIS, is a gray or blackish coloration, caused by the presence of sulphide of iron. The latter is formed by development of sulphuretted hydrogen in the intestine, or by the putrefaction of exudations or tissues. These colorations are oftenest found in the stomach, in old ichorous cavities of the extremities, serous membranes, etc.

d. CALCIFICATION and PETRIFACTION.

(Incrustation.)

MEYER, *Ztschr. f. rat. Med.*, 1851, I. — SCHRÖDER V. D. KOLK, *Nederl. lanc.*, 1853, p. 97.—O. WEBER, *Virch. Arch.*, 1854, VI., p. 561.—VIRCHOW, *Arch.*, 1855, VIII., p. 103 ; IX., p. 618 ; XX., p. 403.—H. MECKEL, *Microgeologie*, 1856.—BECKMANN, *Virch. Arch.*, 1858, XV., p. 540.

Calcification consists either in an infiltration of the tissues and glandular secretions with molecules or large granules, rarely with crystals, especially of carbonate and phosphate of lime, mostly also of like salts of magnesia ; or in the abnormal deposit of the specific secretion of the glands, especially

of the elements of the urine and bile. Thus there appear in the tissues condensations varying in density to the hardness of stone: so-called CALCI-FICATIONS; in the fluids, so-called CONCRETIONS or CALCULI.

1. CALCIFICATION OF TISSUES.

If calcification appears in the tissues, *e.g.* in the basis substance of the costal cartilages, the microscope at first shows the smallest molecules by which the affected parts, *e.g.* the hyaline cartilage substance, become clouded as though by dust. The molecules gradually increase in size; at the same time new molecules are deposited, which also grow. Thereby the structure of the affected part gradually becomes no longer recognizable, while in the part most changed the tissue becomes opaque, and consists entirely of larger or smaller, irregularly angular or rounded granules. These finally fuse together into a homogeneous mass, which by transmitted light shows dark black borders and a brilliant centre; by reflected light, however, it appears as peculiarly whitish, and in which the non-calcified cells are for the most part still perceived distinctly. In this stage there frequently is a reappearance of a certain transparency (as glass, *e.g.*, and crystals pulverized are opaque, but by a more intimate contact of their finest parts, *i.e.* by melting together, they again become transparent). The calcified parts are not colored by carmine, but are colored blue by hæma-toxylin. Fine sections also have a superficial appearance similar to that of bone-tissue, which similarity, however, is not retained on closer scrutiny, and after the addition of reagents.

If to the calcified tissues strong acids, especially muriatic and nitric, be added, they will clear up from the periphery to the centre, and their normal structure will more or less completely return; but parts will commonly be much faded, since these acids always act more or less strongly also upon normal tissues. This clearing up takes place for the most part with a greater or less development of air-vesicles. The vesicles consist of carbonic acid. If this development is great, it is assumed that the deposited mass consists wholly, or for the greatest part, of carbonate of lime; if it is small, phosphate of lime predominates. In almost all cases there is found, besides, a small quantity of other salts of lime, magnesia, etc.

Calcification occurs physiologically and pathologically.

An example of the PHYSIOLOGICAL calcification of tissues is the cerebral sand of the pineal gland and choroid plexus, also, in part, growing bones.

The instances of calcification of cartilage, arteries, etc., in old age, form, as it were, a transition to pathological states.

PATHOLOGICAL calcification affects all parts of the normal organism (especially hyaline cartilage, the valves of the heart, the coats of the vessels, especially of the arteries and capillaries, more rarely of the skin, mucous membranes, serous membranes, muscles transversely-striated and smooth, especially of the arterial wall, tendons, etc.); all tissues (except connective tissue and cartilage, also true and interstitial gland-tissue); the placenta; thrombi, extravasations, exudations, and new-formations of every kind. It affects most often new-formed connective tissue, especially that arising from chronic inflammation in the valves of the heart and in the intima of the arteries, more rarely that in adhesions and pseudo-membranes, in hypertrophies, tumors, etc. Calcification affects cells, *e.g.* cartilage cells, as well as intercellular substance, most often that of cartilage. It is repeated in cells, if these are arranged in layers, the stratification being regular, *e.g.*, in the meninges of the brain, ependyma, choroid plexus, and in the brain-substance

itself. The intercellular substance of cartilage is usually calcified first at a
distance furthest from the vessels.

Concerning calcifications of the placenta, consult CRUVEILHIER (*Anat. path.*, 1829,
livr. I., p. 6 ; livr. XVI., p. 2), SPÄTH and WEDL (*Klin. d. Geburtsk. von Chiari*, u. s.
w., 1858), LANGHANS (*Arch. f. Gynäk.*, III., p. 150), and FRÄNKEL (*Ib.*, II., p.373).
The walls of the capillaries and vessels of the villi are for the most part the parts
of the fœtal placenta especially which are impregnated with lime ; more rarely the
epithelial layer of the villi and their mucous tissue basis substance.   According to
LANGHANS, calcification in the fully-formed placenta forms irregular retiform lines
or small surfaces in the maternal placenta, and fine round processes, which extend
from the latter into the depth of the fœtal placenta, however without reaching the
fœtal surface.   Hence it becomes intelligible that the prosperity of the child is not
essentially injured.   Calcification in the placentæ of immature fœtuses for a long
time dead is, according to FRÄNKEL, confined to fœtal tissue, and is found only in
the finer villi ; these are not calcified throughout their whole thickness, but the lime
is deposited in the wall of the vessels and in their lumen, according to L. only in the
latter place.   Whether this calcification explains the death of the fœtus is still ques-
tionable.

The CONSEQUENCES of calcification are more or less entire loss of function
and of all the remaining properties of the tissues : *e.g.*, in cells of every
kind, most frequently in the epithelium of catarrhal or ulcerated mucous
membrane of the bladder), in the crystalline lens, in muscles, cartilages, in
the valves of the heart.   In the coats of the vessels, especially those of the
arteries, calcification is practically of the greatest importance, because of
the friction and formation of eddies in consequence of the stiffness and un-
evenness, as well as because of the destruction of the elasticity and contrac-
tility of the vessel-wall, the reaction upon the heart (sometimes hypertrophy
of the left ventricle), but especially upon the peripheric distribution of the
vessels (which thereby contain less blood, etc.), not infrequently also be-
cause of their laceration.   A further change of calcified parts is unknown.
Calcification of many tumors, *e.g.*, fibroma, enchondroma, struma, tubercle,
cancers, cysts, as well as extra uterine fœtuses (*lithopædia*), is of advantage
with respect to the whole organism, since it prevents their growth and their
further general influence.

The CAUSES of calcification of tissues are most often those of atrophy,
especially very advanced age.   The disturbances of nutrition which lead to
calcification are mostly local and long continued : many disturbances of the
circulation, chronic inflammation, gangrene.

VIRCHOW (*Arch.*, L., p. 304), when exteriorly on the vertex of the
cranium there were traces of impression or fissure, has often found in the
apparently uninjured parts of the gyri beneath, a great number of ganglion-
cells of the gray cortex calcified.   He accordingly assumes a necrosis, etc.,
from commotion.

The GENESIS of calcification of tissues varies.

In the ordinary calcification of tissues the lime-salts must be brought in
solution into the tissue and there deposited.   Carbonic acid is to be regarded
a solvent of carbonate and phosphate of lime, and is always contained in the
blood in such quantities that the carbonate of lime and at least the neutral
phosphate of lime may be doubled in quantity, both of which salts are solu-
ble.   And yet there are other acids which form soluble salts of lime which
take a part in the transportation of lime into the calcifying tissues (volatile
fatty acids, lactic acid, and glycerin-phosphoric acid).   When they have
reached their destination, the lime-salts must again assume the insoluble
form.   If carbonic acid is the solvent, this process is possible by assuming
that the gas escapes ; on the other hand, lime-salts may be precipitated as

insoluble compounds and so become permanent, and it may be assumed that such precipitates are caused by the higher fatty acids, whose lime-salts are known to be insoluble. The insoluble fat-salt of lime may then be transformed by oxidation into carbonate of lime. Also neutral or basic phosphates of the alkalies may induce this change : for basic phosphate of lime is not at all, the neutral phosphate only very sparingly, soluble.

Sometimes calcification arises in consequence of metastases. In extensive resorption of earthy salts from the bones (extended caries, numerous carcinomata of the bones, etc.), and the prevented excretion of them through the kidneys, the lime-salts, *e.g.*, are deposited in other parts of the organism : most frequently in the pyramids of the kidneys (as infarctions) ; more rarely in the lung-tissue, in the mucous membrane of the stomach, still more rarely in that of the intestine, in the mucous membrane of the ethmoidal and sphenoidal cells, in the dura-mater, liver, in the cerebral vessels. The affected parts thereby assume for the most part a pumice-stone consistency.

KÜTTNER (*Virch. Arch.*, 1872, LV., p. 521) describes a sudden and quickly extending calcification of the inner coat of almost all the arteries of the body, especially the smallest, in a man twenty years old, with scrofulous caries of most of the vertebræ, and with fatty degeneration of the liver, etc.

Deposits of urate of soda occur in arthritis, especially in the articular cartilages, in the neighboring ligaments and tendons, and in the cartilages of the ear ; more rarely in the spongy ends of bones, the skin, kidneys, vessels, and in the interstitial tissue of the pyramids of the kidneys.

Arthritic concretions, according to GARROD (*The Nature and Treatment of Gout*, 1859 ; transl. by EISENMANN, 1861), are originally excreted as a limpid liquid, which is very rich in urate of soda : this crystallizes out, whereby the liquid assumes a milky appearance ; the liquid part becomes gradually resorbed, and thus the exudation by and by becomes permanent and finally hard. Sometimes the concretions contain much phosphate of lime, which probably is the result of a secondary deposit, whilst the urate of soda, acting as a foreign body, gives rise to an inflammation, the product of which becomes chalky. G. found in seventeen out of thirty-seven sick with gout evident gouty deposits : in seven the deposit was perceptible only in the external ear, in nine it was simultaneously in the ear and circumference of the joints, and in only one case were deposits found in other parts of the body without the ear being affected at the same time. The deposits in the folds of the external ear vary in size from that of a pin's head to that of a half pea, are firm or soft, in the latter case containing a creamy liquid, consisting of needles of urate of soda. Consult also HARTMANN, *Ueb. einen Fall von Arthritis urica*, Berl. Diss., 1868.

According to CORNIL-RANVIER, uric acid salts are first deposited in the cells themselves, and afterward in the tissue between them ; according to ZALESKY, in his experiments on birds by ligating the ureters, these salts appear first in the intercellular substance. According to CHRZONSZCEWSKY (*Virch. Arch.*, XXXV., p. 174), the most important quantity of the urates is not formed in the kidneys, but in connective tissue, whence they are carried into the lymphatics (these sometimes appear as if injected with white shining masses), and farther into the bladder.

2. CONCRETIONS, or CALCULOUS FORMATION.

If CALCIFICATION appears in LIQUIDS (secretions), these become first cloudy like lime-water, more consistent, later thick like mortar, and finally are converted into chalky or stone-like masses : calculi or concretions. These vary greatly in size and shape. The latter depends partly upon the form of the cavities inclosing the concretion, partly upon unknown causes. Their surface is smooth or rough. Their consistence is sometimes soft and crumbling, sometimes hard like stone or bone. Their color varies with the essential composition of the concretion, and with the unessential elements, between white, yellow, reddish, brownish-black, etc.

Concretions may be examined MICROSCOPICALLY in thin polished sawed sec-

tions, or in fragments when the former are impossible on account of the crumbling nature of the specimen. In section by transmitted light there are seen in a bright basis substance irregularly rounded, elongated, and otherwise shaped parts of varying size, which sometimes are not unlike bone-corpuscles, but prove to be spaces filled with air, formed in part naturally, in part artificially. In other cases there are seen smaller and larger, wholly irregular fragments, with black contour, which on the addition of acids behave in the manner described.

The CAUSES of the formation of concretions are chiefly catarrhs of the mucous membranes, the presence of foreign bodies, changes in the secretions of glands.

In China, præputial calculi are as frequent as urinary; their cause is the frequently occurring phimosis. (KERR, *New York Med. Jour.*, Mar., 1872.)

The CONSEQUENCES of calculi are: irritation of the skin and mucous membrane (colics due to biliary and renal calculi—catarrhs, ulcerations, perforations), contraction or whole occupation of the space of the inclosing cavity, thereby diminished or arrested function of the tissue of the corresponding gland; more rarely irritation of the bordering serous membranes (peritonitis) or of the adjacent vessels (pyelo-phlebitis).

Calculi sometimes remain a long time in the same condition. Or, after a certain period, they dissolve. At other times they are transformed into other substances: METASCHEMATISM. This is sometimes followed by their spontaneous destruction. Or they are in various ways removed from the organism.

According to MECKEL, gall-stones may either show perpendicular cleavages (radiate), so that they finally are entirely broken up; or they are from without, uniformly or in spots, dissolved by the bile; or both processes occur together. This is also FRERICH's view (*Klin. der Leberkrkh.*, 2. Aufl. II., p. 487). WYSS (*Memorab.*, 1872, 1. H.) describes as another mode of solution for those cases where two or more calculi are present, the grinding together of the calculi, the formation of smooth surfaces (secondary, in opposition to the primary which were present before and grow with the growth of the calculus).

a. CHALKY CALCULI consist chiefly of carbonate and phosphate of lime in varying proportion, of a very small quantity of carbonate of magnesia, water, mucus, albumen, and organic elements; their nucleus is sometimes a foreign body. They are found most frequently in the tonsils, in the vermiform process, in the veins, and in dilated bronchi, and cancers; more rarely in the nose, larynx, uterus, vagina, under the præpuce, etc.

VENOUS CALCULI (*phleboliths*) are for the most part calcified blood, and fibrin clots. But probably they arise in part in other ways (WEDL, *Oest. med. Jahrb.*, 1861). The so-called lung-stones are most often inspissated and calcified secretion of the smaller bronchi; more rarely is it the smallest lobules of the lungs, which, after that they have been affected by catarrhal pneumonia and are calcified, pass outward by a sequestrating suppuration of the surrounding connective tissue: so-called PHTHISIS CALCULOSA.

b. CONCRETIONS OF GLAND-SECRETIONS are: urinary calculi, gall-stones, tartar on the teeth, salivary calculi, pancreatic calculi, lachrymal calculi, prostatic calculi, calculi of the milk-ducts, calculi of the sebaceous glands, so-called seminal calculi. Also to these belong the so-called infarctions of the kidneys.

The urinary and biliary calculi are the most frequent and most important.

URINARY CALCULI, which occur especially in the bladder, arise either from the beginning in the bladder, because the urine, in consequence of its too great acid contents, lets fall free uric acid or urates ; or because it undergoes an alkaline fermentation (this arises through the access of a ferment, or of fungi to the bladder) ; or because the urine-salts are precipitated on solid bodies found in the bladder (pus, mucus, blood, foreign bodies accidentally within the bladder) ; or they come from the kidneys and upper portions of the urinary passages into the bladder and there increase in size.

According to their essential constituents, there are distinguished:

Calculi of URIC ACID AND URIC ACID SALTS: most often round, or rounded, hard, yellow, brown or brownish; rarely white, smooth or somewhat rough; mostly laminated on section.

Calculi of URATE OF AMMONIA only : like the preceding,—rare.

Calculi of the PHOSPHORIC ACID SALTS, especially of ammonia and magnesia, often also of lime: frequent; round or rounded, firm or chalk-like, white, smooth ; for the most part laminated on section.

Calculi of PHOSPHATE OF LIME only : like the preceding,—rare.

Calculi, which consist at the same time of uric acid or urates, and of phosphates, sometimes so that layers of these alternate, sometimes so that one substance forms the nucleus, the other the outside layer ;—frequent.

Calculi, which, besides the salts before-mentioned, contain also CARBONATE OF LIME, which forms sometimes the nucleus, sometimes the outside layer.

Calculi of OXALATE OF LIME : frequent, especially in young persons ; the larger have a warty, even thorny surface (so-called mulberry calculi), a laminated section, are dark brown, very hard ; the smaller are smooth, lighter colored (so-called hempseed calculi).

Calculi of oxalate of lime, surrounded by layers of phosphate of lime or urates.

Calculi of CYSTIN : very rare, small, rounded, yellowish, smooth.

Calculi of XANTHIN : very rare, small, rounded, light brown, smooth.

The larger urinary calculi occur almost always singly, the smaller singly or in numbers, the smallest (so-called URINARY SAND) sometimes in numberless quantity.

RENAL INFARCTIONS are accumulations of salts in the tissue of the kidneys, especially in the pyramids. These lie either in the lumen of the urinary tubuli or in the epithelium, or in the membranes of the former, or in the intermediate connective tissue: the latter is the case in calcareous infarction (KOSTER, *Versl. en Mededeel. der Kon. Akad. von Wetensch.*, 2. R., Deel VI., 1872), the former in the remaining. They sometimes have no signification, sometimes they lead to the formation of larger concrements or to more profound diseases of the kidneys (cysts, etc.).

According to the combination of these, there are distinguished :

INFARCTIONS OF URATES, which consist of uric acid and urate of soda, and often affect the new-born (from the first days after birth to the third and fourth week of life), rarely adults.

CALCAREOUS INFARCTION, which consists of carbonate of lime, according to HOPPE (*Deutsche Klin.*, 1854, No. 14), especially of phosphate of lime, and occurs frequently in more advanced age.

TRIPLE-PHOSPHATE INFARCTION (FRORIEP).

(In VIRCHOW's so-called pigment-infarction large masses of pigment are found in the urinary tubules.)

GALL-STONES occur especially in the gall-bladder, more rarely in the larger and smaller gall-ducts. Their number, size, form. and other properties change with their constituents. The latter are : especially cholesterin and the coloring matter of the bile, especially as bilirubin ; also carbonate and phosphate of lime, mucus, biliary acids, margarin. Gall-stones arise sometimes in consequence of an abnormally increased proportion of cholesterin and biliary coloring matter in the bile ; sometimes precipitation of these substances is facilitated by catarrh of the mucous membranes ; their nucleus is rarely a foreign body. According to METTENHEIMER (*Arch. f. Anat. Phys. u. wiss. Med.*, 1872, p. 509), many gall-stones arise perhaps by inspissation of chalky, etc , substances in the villi, sometimes occurring on the mucous membrane of the gall-bladder.

Usually there are distinguished :

Calculi of CHOLESTERIN : single or few, small or of the size of an egg, mostly round or oval, smooth or in various ways granulated, whitish or yellowish-brown ; rarely angular ; always with crystalline striation of the surfaces of fracture or section.

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Calculi of CHOLESTERIN and BILIARY COLORING MATTER, with small quantity of carbonate and phosphate of lime, in various proportions of these constituents: most frequent; brown or green; of different sizes; for the most part many; round or angular; smooth; with chalky section like the external surface or variously colored in the different layers.

Calculi of BILIARY COLORING MATTER alone (rare): brown or green; small; less numerous; round or pointed.

Calculi of CARBONATE OF LIME alone: light; rough; with crystalline fracture.

I found in the seminal vesicles of a kyphotic person, about forty years old, a formation probably representing a lower grade of SEMINAL CALCULI. It was about .3 mm. in diameter, rounded, somewhat flattened, and consisted of a homogeneous, dense substance, not affected by acetic acid and alkalies, and of numberless spermatozoa. The latter lay partly in the formation, in part the bodies only were found, while the tails, tuft-like, projected from the periphery.

e. LARDACEOUS, OR AMYLOID DEGENERATION.

(Waxy degeneration, cellulose degeneration, vitreous swelling, hyaloid degeneration, VIRCHOW'S degeneration.)

ROKITANSKY, *Hdb. d. path. Anat.*, 1842, III., p. 311, 384, 417, 424; 1846, I., p. 445; *Sitzgsber. d. Wien. Acad.*, 1854, XIII.—CHRISTENSEN, *Copenh. Ugeskr.*, 1844. —MECKEL, *Charité-Ann.*, 1853, IV., p. 264.—BUSK, *Quart. Journ. of Micr. Sc.*, 1854, No. VI., p. 101.—GAIRDNER, *Ed. Monthly Journ. of Med. Sc.*, 1854.—SANDERS, *Monthly Journ.*, 1854.—VIRCHOW, *Arch.*, 1854, VI., p. 268 et 416; VIII., p. 140 et 354; XI., p. 188; XIV., p. 187; XV., p. 232; *Würzb. Verh.*, VII., p. 222.— MOLESCHOTT, *Wien. Wochenschr.*, 1855, No. 9.—FRIEDREICH, *Virch. Arch.*, X., p. 201 u. 507; XI., p. 387; XV., p. 50; XVI., p. 50.—LOEPER, *Beitr. z. path. Anat. d. Lymphdr.* Würzb. *Diss.*, 1856.—WILKS, *Guy's Hosp. Rep.*, 1856, II.—PAGEN-STECHER, *Die amyl. Degener.* Würzb. *Diss.*, 1858.—KEKULÉ, *Heidelb. Jahrb.*, 1858. —BECKMANN, *Virch. Arch.*, 1858, XIII., p. 94.—C. SCHMIDT, *Ann. d. Chem. u. Pharm.*, 1859, CX., p. 250.—NEUMANN, *Deutsche Klin.*, 1860, Nr. 35, 37 et 39.— *Arch. d. Heilk.*, 1868, p. 35—PLEISCHL and KLOB, *Wien. Wochenschr.*, 1860.— LAMBL, *Aus. d. Frz.-Jos.-Kinderspit.*, 1860, p. 311.—E. WAGNER, *Arch. d. Heilk.*, 1851, II., p. 481; VII., p. 569.—HERTZ, *Greifsw. med. Beitr.*, 1863, p. 93.—RUD-NEFF and KÜHNE, *Virch. Arch.*, 1865, XXXIII., p. 66.—FEHR, *Ueb. d. amyl. Degen. insbes. d. Nieren. Diss. Bern.* 1866.—KYBER, *Stud. üb. d. amyl. Degen.*, Dorpat, 1871.

LARDACEOUS or AMYLOID DEGENERATION is for the most part a chronic, almost always a secondary filling of the tissues (especially the small arteries and capillaries, more rarely also other elements) with a peculiar homogeneous substance, having a dull lustre, translucent, almost always colored characteristically by iodine and sulphuric acid, but albuminous, which substance in high degree causes ischæmia of the parts, induces emaciation of the surrounding tissues, diminishes or arrests the function of the organ affected, for the most part induces anæmia of high-grade with general marasmus, and (in higher grades) is never curable.

Lardaceous degeneration is next to fatty metamorphosis the most important and most frequent degeneration. Its reaction on the whole organism is, because of its for the most part great extension, greater than that of every other degeneration.

Lardaceous degeneration occurs oftenest in the lymph-glands, spleen, liver and kidneys. Next in order are the mucous membrane and submucous tissue of the digestive canal, omentum, and supra-renal glands. This form of degeneration is more rarely found, and almost always in much less degree, for the most part simultaneously with that of the organs above mentioned, in the other coats of the digestive tract from the mouth to the anus, in the pancreas, in the mucous membrane of the bladder, in the prostate gland, in the uterus and vagina, in the ovaries, testicles,

heart, in the vasa vasorum of the aorta, in the small veins, in the thyroid-gland (*struma amyloidea*), in the bronchi and lungs, in some nerves, in adipose tissue; in blood-coagula. Not infrequently fibrin-casts also are found lardaceous in kidneys affected by lardaceous degeneration.

Lardaceous degeneration in the vessels of the external muscles of the body and skin is very rare; it has not yet been observed in those of the bones.

The order in which the various organs become thus affected, has not yet been accurately determined. Probably in suppuration of long standing the lymphatics are first affected and then the remaining organs. It is likewise unexplained, why, in cases apparently alike, at one time the spleen, liver and kidneys are affected to an almost equal extent, while at another time one or another of these organs are affected and the integrity of the others is preserved.

Slight degrees of lardaceous degeneration cannot be perceived by the naked eye. Higher degrees, on the other hand, change the organs, especially the liver, spleen and kidneys, less the lymph-glands and mucous membranes, in a characteristic manner. These changes consist in slight, moderate, or great enlargement of the organs, with preservation of the normal shape, or with a thickening of their normally sharp borders; in a peculiar gray or pale-gray coloring; in a homogeneous, tolerably dry, strongly translucent appearance, and in a tough, doughy consistence. These conditions belong to the whole organ uniformly, or to certain parts of it chiefly; *e.g.*, the follicles in the spleen, the cortical substance alone in the kidneys, the medulla in the supra-renal capsules, etc. The blood-contents of the part (as well as of the whole body) are diminished almost always to a great degree; the blood flowing out of the larger vessels after section is mostly bright and fluid. The organs decompose with difficulty.

These peculiarities are obliterated to a greater or less degree, if the organs were beforehand, or becomes simultaneously diseased in other respects. The most frequent changes are fatty infiltration and fatty metamorphosis of the cellular elements (liver and kidneys), hypertrophy of connective tissue (kidneys, etc.), increased blood-supply, and increase of pigment (various organs).

The microscope, or the reaction by sulphuric acid and iodine, is employed to recognize lardaceous degeneration of parenchymata, in its lower grades, as well as that of membranous organs, or of conjunctive tissue.

Lardaceous degeneration is characterized MICROSCOPICALLY, by more or less increase of the diameters of the tissues affected; by their peculiarly light, homogeneous, dull appearance, and characteristic coloring by iodine and sulphuric acid; and by the fact that the former granular condition of the cell-contents, as well as the nucleus, cell-membrane, etc., are no longer demonstrable.

Lardaceous degeneration affects SMALL ARTERIES and CAPILLARIES oftenest, and earlier than all other tissues, much more rarely the veins. This form of degeneration is at once most characteristic in the vessels. The diameter of the capillaries is doubled, and more; no nuclei are to be found in their walls; their lumen is more or less contracted, not infrequently becoming entirely closed. Lardaceous degeneration affects the small arteries in a similar manner: here the intima, with the endothelium and the muscular coat, and rarely the adventitia also, are probably affected nearly at the same time; also the membranæ propriæ, *e.g.*, the urinary tubules. In the much more rare lardaceous degeneration of cells, as of glandular cells, nuclei and cells of the tissue of the spleen and lymph-glands, the former at first increase in diameter and are more granular; thereupon they again become light,

homogeneous, dull, are more firmly united to one another or blend together; the nucleus disappears, or is no longer visible. Finally, the cell becomes transparent and bright, and is very brittle, easily breaking up into smaller fragments. Lardaceous degeneration of connective tissue is still in question.

KYBER holds with VIRCHOW that the muscular coat in small arteries is the chief seat of the degeneration; but in many organs it is almost as often the intima. Only in the omentum has KYBER found a continuous extension of the degeneration from the small arteries through the capillaries to the veins. In the heart, KYBER found degeneration of the endocardium, also of the auriculo-ventricular valves, as well as of the muscular tissue (rarely of the substance of the muscle itself, for the most part of the sarcolemma). Lardaceous degeneration often affects also the trunks and large branches of arteries and veins : of the former the aorta and pulmonary arteries to the greatest extent and earliest, besides those given off from the arch of the aorta, never those beyond the axillary and common carotid arteries, never the femoral. In the large arteries, the middle layers of the intima, single groups only of muscle-cells in the muscular coat, the nutrient vessels in the adventitia are affected. In the vena portæ and hepatic veins, the degeneration is often general, without a single hepatic capillary being affected.

According to ARMAUER-HANSEN (*Beitr. z. Anat. d. Lymphdr.*, 1871), there are two kinds of amyloid degeneration of the lymph-glands : in the one the bloodvessels chiefly degenerate, in the other the sinus (lymphatic vessels?). The spleen shows the same relations. In " sago-spleen " only the parenchyma of the arterial sheaths (Malpighian bodies and simple cytogenic sheaths) is lardaceous ; the parenchyma of the spleen is normal. On the other hand, in diffuse lardaceous spleen the latter is lardaceous : a thin tunic of lardaceous substance is first shown in the neighborhood of the capillaries and the veins ; the spindle-shaped cells lying nearest the lumen of the veins are not lardaceous ; on the other hand, the limiting fibres of the net-work and the intermediate substance are lardaceous. The sheath of the arteries is free, but may later also become degenerated. (KYBER, *Arch. f. micr. Anat.*, 1872, VIII., p. 568.)

ROKITANSKY (*Hdb.*, 1855, I., p. 329), as well as LAMBL and NEUMANN (l. c.), found lardaceous degeneration also in the muscular elements of the intestinal wall, and in the muscular substance of the villi, in the *muscularis mucosæ*, and in the proper muscular coat of the intestines. The muscle-fibres become broader, their nucleus indistinct, and they appear to blend together, and easily break up into irregular flakes.

HAYEM (*Gaz. méd. de Par.*, 1866, No. 6) found amyloid degeneration also in connective tissue, and very rarely in fat-cells. According to KYBER, the degeneration affects the fat-tissue between the fat-lobules and the septa between the fat-cells, sometimes only the nuclei, sometimes also the fibres ; also, according to HAYEM, the membrane.

The lymphatic vessels in the vicinity of capillaries which have suffered lardaceous degeneration, are for the most part strongly contracted ; the gland-cells, if they are not themselves degenerated, show all grades of simple atrophy to complete disappearance, partly in consequence of diminished or wholly interrupted supply of arterial blood, partly in consequence of compression.

The reaction of the material of lardaceous degeneration is especially characteristic. Degenerated parts, cleaned as far as possible of blood, receive a peculiar brownish-red color (like mahogany) by iodine (solution of iodine in water, or diluted tincture of iodine, or solution of iodide of potassium), while parts not degenerated are colored yellow. After the addition of dilute or concentrated sulphuric acid, they immediately or after minutes and hours, receive a violet, rarely a blue color, which then either remains unchanged for hours and weeks, or after a short time again disappears. The reaction on the fresh organ affords to the naked eye a dark violet or black color. If the parts are mixed with the usual albuminate, there ap-

pears a bluish-green or green color. (Sometimes the reaction succeeds only after repeated trials.) The remaining reactions afford nothing worthy of note; water leaves the lardaceous substance unchanged; acetic acid diluted has no effect; concentrated, it causes the substance to somewhat swell up; concentrated alkalies dissolve it; alcohol and ether are without effect.

While iodine and sulphuric acid are usually necessary to bring out the characteristic color of the lardaceous substance, FRIEDREICH describes a case where, after the addition of iodine alone in the spleen affected by lardaceous degeneration, in the pulp as well as in the follicles, there arose a deep blue or violet blue color, which caused FR. to assume, besides the amyloid, an amylous tumor of the spleen.

With respect to the nature of lardaceous degeneration, it was believed that the combination of lardaceous substance could be recognized by the reaction by iodine and by iodine and sulphuric acid, although the disease had for a long time been called albuminous obstruction, albuminoid infiltration. The English called it waxy degeneration; BUDD, colloid degeneration; MECKEL, on account of the similarity of the reaction, etc., cholesterin degeneration; VIRCHOW introduced successively the names cellulose degeneration, lignification, and amyloid degeneration; O. WEBER calls the disease vitreous swelling, or hyaloid degeneration, or hyalinosis.

Most of these names and theories have been shown to be untenable, since two elementary analyses, made by different chemists on different lardaceous organs, led to an altogether unexpected disclosure. KEKULE's investigations on a lardaceous spleen of highest grade showed : that it contained a considerable quantity of cholesterin, but that the latter is not the cause of the reaction by iodine and sulphuric acid ; that it contains no body similar in a chemical point of view to starch, or cellulose ; that the agreement of the combinations of this substance with albuminous substances is so great that, as in a body of a kind which does not allow of an absolute clear representation, it is only possible that lardaceous substances are peculiarly modified and changed albuminoid materials. According to C. SCHMIDT's analysis, made likewise on a lardaceous spleen, the amyloid is not a hydro-carbon free from nitrogen, but a nitrogenous albuminate.

Lardaceous degeneration is most probably a retrograde metamorphosis of albuminates, the lardaceous substance is probably an intermediate step between the latter and fat and cholesterin. There are perhaps many such intermediate steps. The nitrogenous contents of lardaceous substance only show that nitrogen is present, but they do not show that it is in form of an albuminous body. MECKEL's investigations showed the abundance of cholesterin.

RUDNEFF and KÜHNE freed lardaceous substance from all fixed albuminous matters, by digesting it with artificial gastric juice, until the latter no longer took up peptone at 40° C. Accordingly, its composition also agrees with that of albumen, but shows some opposing reactions. Its composition appears more essentially complicated than that of albumen.

DICKINSON (Med. Times and Gaz., 1868, No. 951) found in comparative investigations of healthy livers and those with lardaceous degeneration, that the latter was decidedly poorer in alkaline salts than the former. The average loss amounted to almost a fourth of the normal quantity of saline ingredients. From this and on account of the ætiology of lardaceous disease, D. concludes that it consists essentially only in a want of alkalies in the tissues.

Whether lardaceous substance arises by metamorphosis of common protein substances, or whether it is deposited in consequence of a metastasis, has not as yet been determined. RINDFLEISCH includes the degeneration among the so-called infiltration-states : an albuminous body of the nutritive liquid is detained on its way through the tissues and is excreted in solid form. To this is referred also the early disease of the smallest arteries and capillaries.

With as great difficulty can it be decided whether lardaceous substance, reacting in a similar manner with iodine and iodine and sulphuric acid, is analogous to a substance occurring in the cells and basis substance of many cartilages (VIRCHOW), especially often of the tracheal cartilages (KYBER), of the cartilages of a spheno-occipital ecchondrosis (KLEBS), as well as in old fibrinous coagula (FRIEDREICH). Lardaceous substance has probably nothing in common with the *corpora amylacea*, colored blue by iodine alone, with peculiar bodies which VIRCHOW found in the vessels of the retina and gall-bladder, with myelin, etc.

Diseases, in consequence of which lardaceous degeneration appears, are

almost always those in which suppurations of long duration occur in the
bones or soft parts, for the most part with evacuation of the pus and debris
of tissues; at the time of death pus is for the most part still flowing, some-
times it has been dried up for years. The primary affections here are,
chiefly: caries of one or more bones, chronic ulcerous tuberculosis of the
lungs, often with chronic ulcerous tuberculosis of the intestines; more
rarely chronic ulcers of the soft parts, especially simple or tuberculous ulcer
of the intestines, simple cutaneous ulcers, chronic syphilitic ulcers of the
skin or intestinal canal, urinary fistulæ of long duration, chronic psoas
abscesses, bronchiectasiæ, chronic pyelitis, ulcerating carcinomata, etc.
Much more rarely is lardaceous degeneration found in consequence of con-
stitutional syphilis without long-continuous suppuration, as well as in con-
sequence of exhausting diarrhœas without intestinal ulcers. Finally, it
occurs very rarely in constitutional syphilis without suppuration (also here-
ditary), in leucocythæmia, typhoid fever, in rachitis, obstinate malarial
fevers, organic diseases of the heart. It has been observed primarily only
in the form of so-called Bright's disease.

Lardaceous degeneration is in the greater number of cases a chronic dis-
ease, sometimes extending through many years, as it certainly follows from
clinical observation. In many rarer cases the duration is much shorter,
lasting even only one or few months. The causes of lardaceous degenera-
tion have not as yet been disclosed.

Many of our own observations, as well as the three made by COHNHEIM (*Virch.
Arch.*, 1872, LIV., p. 271), indicate that lardaceous degeneration may be developed
in 4–6 months.

The CONSEQUENCES of lardaceous degeneration are on this account with
greater difficulty determined, since it arises primarily with extreme rarity,
since the consequences of the primary affection and those of the lardaceous
disease are in part the same, and since, finally, lardaceous degeneration of
the vessels in glandular organs is followed by secondary affections of the
glandular epithelium (simple atrophy and fatty metamorphosis). They are
especially diminution of arterial blood-supply, and diminished or wholly
suspended normal transudation, as well as the effects of pressure of the
thickened vessels on the circumjacent lymph-capillaries and gland-cells. The
consequences of lessened nutrition attract but little attention, with the
exception of individual organs, as of the intestine, very rarely also of the
liver, where in consequence of lardaceous degeneration, peculiar so-called
lardaceous ulcers arise. Lessened nutrition is, however, followed farther on
by diminished function. This becomes the more striking, as lardaceous
degeneration especially affects glandular organs. The disturbances of func-
tion consist partly in interrupted blood-formation (in lardaceous disease of
the liver, spleen, lymph-glands, intestinal mucous membrane), and from
this, in anæmia, hydræmia, marasmus, dropsy; they are partly disturb-
ances of specific function, *e.g.*, of the liver, kidneys, intestinal mucous
membrane, but which clinically are as yet but little known.

Lardaceous degeneration limited locally has been observed but a few times: in
cartilage, also in new-formed tissues (VIRCHOW), in lymph-glands (BILLROTH), in
mesenteric glands after typhoid fever (HIRSCHFELD), in a soft connective tissue
tumor of the lower eyelid (KYBER, l. c., p. 111). LINDWURM and BUHL (*Ztschr.
f. rat. Med.*, 1862, XIV., p. 257) observed HYPERTROPHY AND ULCERATION OF THE
SKIN WITH AMYLOID DEGENERATION in a man fifty-four years old. The skin of the
whole body had been affected about thirteen years. The affection resembled *pity-*

riasis rubra, lichen ruber, ichthyosis hystrix s. cornea, ichthyosis simplex ; the surface of the body bore 50–60 ulcers. Not only the latter, but also the entire skin were painful. (See also KYBER's cases, l. c., p. 134.)

HAYEM (l. c.) saw amyloid degeneration in the intestinal canal extend through the whole thickness of the wall, corresponding especially to the follicles, so that finally there appeared amyloid erosions and ulcerations. According to COLBERG (*D. Arch. f. klin. Med.*, 1867, II., p. 478), ulcers without any combination with tuberculosis, often occur in amyloid intestinal mucous membrane. They begin on the summit of the villi, dependent upon mechanical irritation of the ingesta, especially if the latter—in simultaneous lardaceous degeneration of the kidneys—are mixed with urinous products of decomposition.

BUHL (*Lungenentz*, etc., 1872, p. 59) describes a lardaceous cirrhosis of the lungs ; the capillaries and smallest arteries are degenerated, the interlobular connective tissue is thickened by cell-growth.

The TERMINATION of lardaceous disease in its higher grades, which only are to be diagnosticated with certainty, is with rare exceptions FATAL. Slight degrees of it, on the other hand, which almost entirely escape recognition, may doubtless be CURED, with the removal of the cause, *e.g.*, of ulcerous secondary syphilis. The kind and manner of cure is wholly unknown.

The following points serve for the DIAGNOSIS of lardaceous disease in general : 1. with respect to the causative disease (*vide supra*) ; 2. the enlargement of the liver and spleen, as well as that of the lymph-glands and kidneys, which is rarely demonstrable ; 3. the symptoms of anæmia, wasting and cachexia, which in its long duration are rarely absent ; 4. dropsy of the lower extremities, which is seldom absent, as well as general dropsy, which occurs in almost half of the cases ; 5. the absence of other causes of congestion. On account of lardaceous degeneration of the kidneys occurring mostly at the same time, the urine usually exhibits characteristic changes, so much the more, if other renal disorders, especially those dependent upon affections of the heart, may have been excluded ; the urine for the most part has an increased specific gravity, its coloring matter is greatly increased ; the urine is clear and mostly albuminous, but the albumen occasionally disappears ; it contains probably characteristic casts ; the quantity of the urine is at first usually increased, but later diminishes (TRAUBE, ROSENSTEIN, and others). Finally, abundant watery diarrhœic stools occur on account of the frequent simultaneous existence of intestinal ulcers, as well as on account of the often present lardaceous degeneration of the vessels of the intestinal mucous membrane.

CORPORA AMYLACEA, AND LAMINATED AMYLOID BODIES.

PURKINJE, *Ber. üb. d. Prag. Verh. d. Naturf.*, 1837.—VIRCHOW. *Arch.*, VI., pp. 135 u. 416.—DONDERS, *Nederl. Lanc.*, 1854, I., 24.—FRIEDREICH, *Virch. Arch.*, 1856, IX., p. 613 ; X., pp. 201 and 507.—PAULIZKY, *Ib.*, XVI., 147.

CORPORA AMYLACEA are commonly ranked with lardaceous degeneration, although they have nothing in common other than in part the reaction with iodine, or with iodine and sulphuric acid. But they are probably also nitrogenous.

The bodies mentioned are very small, or macroscopical, round, oval or irregular, homogeneous or concentrically laminated, in varying number and regularity, dull bodies. Most of them become blue or bluish-gray by iodine alone, or receive a beautiful blue coloring by the addition of sulphuric acid ; many, in consequence of a combination with more nitrogenous substances, become only green, others finally, only brown or yellow. Hot water, as well as caustic alkalies, gradually dissolve these little bodies, while alcohol and ether effect no change. Their transformation into sugar has not yet been accomplished. The laminated amyloid bodies

of the prostate often contain in the centre cells or nuclei, or forms similar to these, those of the lungs often particles of carbon, or blood-corpuscles.

Corpora amylacea are most frequent in the nervous system, and above all, where the so-called neuroglia is found, especially also in the ependyma of the ventricles, especially if this is thickened, in the white substance of the brain (in chronic mental diseases, atrophy of the brain, etc.), in the same parts of the spinal cord (in high degree in the so-called tabes dorsalis), in the pituitary body, in the choroid plexus, in atrophic nerves of every kind, especially in the optic nerve, and in the retina ; also in the prostate, where they reach their greatest volume, since here many such bodies often have a common envelope, as well as in the urino-genital mucous membrane ; finally in the lungs, in the gall-bladder, and in rare cases in many epithelia of mucous and serous membranes, in cicatrices of the skin, in the interior of phleboliths, in osteomalacial bones, in pus, in cellular new-formations, *e.g.*, cancers.

Almost regular, distinct, concentrically laminated, otherwise little changed carti-lage-cells, which by iodine receive a beautiful rose-red or half-violet color, are found in the cartilages, especially the intervertebral, more rarely in other articular carti-lages, during the changes of old age and in caries. (LUSCHKA, VIRCHOW.)

Corpora amylacea for the most part show no further changes ; sometimes they become calcified, even to so great an extent that in the nervous sub-stance stony masses of varying size appear ; these, in the prostate, are sometimes colored brown or black.

In the brain of an old epileptic and imbecile man, I found, near the posterior horn of the lateral ventricle, an irregularly rounded body, of stony hardness, of the size of a cherry, with a rough surface like sandstone, and near this a body partly of the hardness of stone, partly of less firm consistence, of the size of a bean. These con-sisted of large, round or oval, concentrically laminated formations, which were com-pletely calcified. All the surrounding vessels were to a great degree calcified ; the substance of the brain here contained numerous, for the most part large corpora amylacea, surrounded by a substance rich in nuclei, and homogeneous, or indistinctly fibrous.

The ORIGIN of corpora amylacea is always the consequence only of a local, never (like lardaceous degeneration) of a general affection. These bodies are probably not the causes of atrophy, but only consequences of it. Their more intimate relations are unknown.

MYELIN.

MYELIN is a body, like the medulla of nerves, arising mostly from nerve-substance, and which is characterized especially by its peculiar forms and peculiar dull lustre. It exists most often as simple formations of various size, round, oval, filamentous, knot- or club-like, etc., but for the most part with double contour, sometimes concentrically striated.

Myelin, discovered by VIRCHOW (*Arch.*, 1854. VI., p. 562 ; VIII., p. 114), as it is observed in the microscopical examination of tissues, shows the following chemical properties : It swells up greatly in water. Hot alcohol, ether, chloroform, oil of turpentine easily dissolve it. Weak acids and alkalies exert no effect ; strong alka-lies cause it to shrivel somewhat, and later to assume its characteristic appearance ; strong acids, especially concentrated sulphuric acid, cause it to swell up still more, and later destroys it. Chromic acid, in strong concentration, makes it yellow, hard

and stiff; tincture of iodine imparts a faint iodine-brown color. Sulphuric acid, concentrated, colors it red, sometimes violet. With concentrated solutions of salt, it shrivels up.

These reactions of myelin (swelling and peculiar forms) proceed not from undecomposed nerve medulla, and not even from one single substance. O. LIEBREICH ($Virch. Arch.$, XXXII., p. 387) showed that neither protagon ($C_{23}H_{241}NPO_{44}$), nor one of its products of decomposition (glycerine-phosphoric acid, fatty acids, neurin) arising from the action of alkalies furnish of themselves myelinic forms, but that these are beautifully obtained by the addition of an alkali (neurin, potassa, soda, etc.) to a mixture of protagon and fatty acids (thus protagon in the presence of a soap); a product of decomposition (free from phosphorus) arising by boiling protagon (containing phosphorus) with hydrochloric acid, furnishes with the same treatment the same myelinic forms. Also H. KÖHLER (Ib, XLI., p. 265), who in his investigations of brain substance arrived at other conclusions than L., found, that no element of the brain in the undecomposed and pure state in water, assumes myelinic forms; on the other hand, the product of decomposition described by him as neurol acid ($C_{100}H_{30}PO_{34}$), and his myelo-margarin ($C_3H_{56}O_{10}$), if it is contaminated by cholesterin, swell up on the addition of water in the form of myelin. The chemical nature of both substances is moreover not yet sufficiently established. Since now, according to DIAKONOW, protagon is a mixture of lecithin ($C_{84}H_{80}NPO_{18}$) with cerebrin, and lecithin with water assumes the form of myeline, so the reactions of myelin may depend upon either lecithin or decomposed protagon. Moreover, BENEKE has shown that a solution of cholesterin in soap, and NEUBAUER, that oleic acid furnish myelin forms by the addition of ammonia; the protagon of LIEBREICH, which in contact with a soap showed myelin forms, was free from cholesterin.

BUHL ($Lungenentz$, etc., 1872, pp. 51 and 62) describes a myelinic degeneration of the epithelium of the lungs in, by him so-called, desquamative pneumonia.

$f.$ COLLOID METAMORPHOSIS.

Colloid metamorphosis consists in the transformation of tissues into a completely homogeneous, colorless or faint yellow, dull, translucent, sometimes fluid or soft-like glue, sometimes more solid, but always easily fragile substance, which mostly dissolves in cold and hot water, for the most part not in alcohol and ether, in caustic alkalies, and is not changed by acetic acid, and iodine and sulphuric acid. The substance formed, so-called COLLOID, is, like lardaceous matter, a MODIFIED (with hydro-carbon) PROTEIN-SUBSTANCE (albuminate of soda). It has not a single positive character: it is distinguished from albumen by its insolubility in acetic acid, from mucus by the extent of coagulation with acetic acid, from lardaceous substance by the want of color with iodine and sulphuric acid.

According to EICHWALD ($Würzb. med. Ztschr.$, 1864, V., p. 270), colloid is modified mucous substance, since its reactions gradually pass into those of true mucous substance. The material of colloid globules, mucin, colloid matter, and mucous peptone are distinguished almost only by the varying ease with which they pass from a soft to a liquid state: they are dissolved by dilute alkalies, but are restored by acids; they are soluble in mineral acids: like all protein substances they are precipitated by alcohol, they furnish Millon's test, etc. According to SCHERER ($Ibid.$, 1866, VII., p. 6) mucin, metalbumen, and colloid substance stand in a similar relation to one another, as casein, albumen and fibrin. Dissolved mucin, like soluble casein, is always combined with alkalies and is precipitated by acids from these combinations. Others hold colloid to be albumen, which has become insoluble in acetic acid, on account of the presence of considerable quantities of chloride of sodium. According to SCHERER's older, and OBOLENSKY's ($Arch. f. d. ges. Phys.$, 1871, IV., p. 336) more recent investigations, mucin from the fluid of cysts, like that from the submaxillary glands, contains C_{52}, H_7, N_{12}, O_{26}.

Colloid metamorphosis affects cells chiefly, especially epithelial cells; more rarely other parts of tissues, especially muscle-fibres.

1. Colloid metamorphosis of cells.

Microscopically, the cell either is in its entire mass bright, since under simultaneous enlargement there appears a bright homogeneous substance in place of the granular contents. Or, there is formed in the granular cell-contents bright, sometimes faintly violet, homogeneous, round points, which gradually become larger, press the granular cell-contents to the periphery, finally reach the latter itself, waste it and thereafter escape. Or there arise many such points, which later coalesce within the cell. The cell-nucleus is thereby either simply atrophied, or undergoes fatty degeneration. Finally, colloid metamorphosis rarely begins in the nucleus, which then gradually becomes larger, bright, homogeneous, reaches the cell-membrane and causes it to disappear. In all cases, the cell is destroyed by this metamorphosis. The colloid is at first for the most part fluid, and then coalesces with the same substance having its origin in other cells. It is more rarely solid when it leaves the cell, and then remains always, wholly or in part isolated: there arise the so-called colloid masses, or colloid granules, *i.e.*, for the most part flat, homogeneous masses of varying size, and of rounded, or round and pointed, or entirely irregular form.

Yet other colloid formations often occur. These are slightly or much, regularly or irregularly concentrically laminated; sometimes, besides a central concentric stratification, or without it peripherically, they show a radiating striation, whereby the surface is regular or bristling in the direction of the radii; sometimes radiations, far from or close to one another, pass regularly from the centre to the periphery. Sometimes all these formations are surrounded by a common enveloping mass.

A fatty metamorphosis, simultaneously with colloid metamorphosis, is also not infrequently found in the same cells, sometimes with cholesterin formation, or calcification, or a filling with diffuse or granular pigment.

The occurrence of colloid metamorphosis of cells affects normal as well as pathological tissues: especially the thyroid gland and choroid plexus. Their slight grades are recognizable only through the microscope. In higher grades, it causes an enlargement of the tissues, anæmia of them, and filling with a substance like fluid glue or boiled sago, uniformly distributed or inclosed in cyst-like spaces.

The consequences of colloid degeneration of the cells are mostly slight, since they usually give rise to only moderate swelling of the affected parts.

In the thyroid gland, where the epithelial follicles are the seat of this metamorphosis, the follicles become enlarged to a varying extent, remain so permanently, or coalesce after atrophy of the stroma. The metamorphosis affects normal, as well as new-formed tissue of the thyroid gland, and gives rise, especially in the latter, to the sometimes very large examples of so-called GOITRE (*struma lymphatica s. colloides s. gelatinosa*). According to VIRCHOW, on the other hand, colloid of the thyroid gland does not have its origin in the gland-cells, but in the free fluid of its follicles, in the contents escaped or become free by destruction of the cells. It is formed, when these substances are brought into contact with a large quantity of soda or salt. V. distinguishes two modifications of it: one is dissolved in a large quantity of water and behaves in this solution like an alkaline solution of albumen; the other is not wholly soluble even in boiling water, not even in acetic and hydrochloric acids, becomes violet by the latter, completely solid by alcohol. Both forms may be artificially represented, if large quantities of salt be added to a fluid which contains albuminate of soda (*i.e.*, albumen, which is soluble by caustic or carbonate of soda). Colloid or gelatinous granules are therefore concretions.

The epithelial cells of mucous and serous membranes likewise sometimes suffer colloid degeneration. The simple pouched and lobulated glands, especially of the uterine cervix, prostate and lips, the urinary tubuli and Malpighian bodies of the

cortex of the kidneys, the anterior lobes of the pituitary body, and the cortex of the supra-renal capsules, for the most part in less degree numerous other glands, become by colloid degeneration of their epithelium transformed into so-called COL-LOID CYSTS. (See Cyst-formation.)

In *Arch. d. Heilk.*, VII., p. 463, I communicated a peculiar case of colloid degeneration of the sebaceous glands of the face, so-called COLLOID MILIUM OF THE SKIN. SLAVJANSKY (*Virch. Arch.*, LI., p. 470) describes a colloid metamorphosis of the *membrana granulosa*, whereby the ovum was finally covered by a homogeneous shining mass.

The CHOROID PLEXUS is transformed by colloid metamorphosis of their connective-tissue cells by new formed nuclei, into the known aggregations of colloid cysts.

Colloid metamorphosis is sometimes found in the endothelium of the BLOOD-VESSELS. WEDL (*Wien. Acad.-Ber.*, 1864, XLVIII.) also describes in the walls of small vessels colloid deposits, which, free externally, are prominent on the surface, or are surrounded by a capsule. ROKITANSKY (*Lehrb*, p. 472), ARNDT (*Virch. Arch.*, 1868, LI., p. 461), MAGNAN, transl. by ERLENMEYER (*Arch. d. d. Ges. f. Psych.*, 1871, XVII., p. 303) describe peculiar "colloid" degeneration of the cerebral vessels in general paralysis.

NEUMANN (*Sitzgsber. d. Wien. Acad.*, 1869, LIX. ; *Allg. Wien. med. Z.*, 1870, No. 32) describes a colloid degeneration in the CUTIS of old people : its fibrous bundles become wholly invisible and replaced by a homogeneous coagulated mass like glue. Nerves and vessels appear to be entirely destroyed. A somewhat similar thing was found by N. in *elephantiasis Græcorum*.

Probably a series of peculiar formations, not infrequently occurring, which have many things in common with colloid masses, do not belong to colloid : *e.g.*, in the ganglion-cells of the retina, in those of the brain substance, etc.

Concerning colloid metamorphosis of NEW-FORMED CELLS, see below.

SCHRANT, *Tijdschr. d. Nederl. Maatsch.*, 1852, et *Arch. f. phys. Heilk.*, IX.; *Arch. f. d. holl. Beitr. zur Natur- u. Heilk.*, 1858, I., p. 169.—LUSCHKA, *Arch. f. phys. Heilk.*, 1854, p. 9.—VIRCHOW, *Würzb. Verh.*, II. ; *Unters. üb. d. Entwickelung d. Schädelgrundes*, 1857 ; *Die krankh. Geschw.*, III., p. 2.—E. WAGNER, *Arch. f. physiol. Heilk.*, 1856, XV., p. 106.—HAECKEL, *Virch. Arch.*, 1859, XVI., p. 253.—RINDFLEISCH, *Lehrb. d. pathol. Gew.*, 1871, pp. 24 u. 30.—NEUMANN, *Arch. d. Heilk.*, 1868, IX., p. 364.

2. COLLOID METAMORPHOSIS OF MUSCLES.

Colloid metamorphosis of transversely striated muscle-fibres is for the most part acute, seldom chronic : constant in typhoid fever, especially in the adductors of the thigh, abdominal recti, diaphragm, in less degree in the greater thoracic, in other muscles ; frequent also in typhus fever, acute miliary tuberculosis, scarlet fever, small-pox, uræmia, etc., in all severe fevers. It occurs as a local process in convulsive muscular affections (tetanus), trichinosis, extensive freezing, in many cases of myocarditis, very commonly in muscular cancer. It is perhaps very rarely a primary affection.

ZENKER (l. c.) first demonstrated the constant occurrence of the affection in typhoid fever, and described it most accurately. It was earlier observed by BOWMAN and VIRCHOW under other circumstances. I observed (*Arch. d. Heilk.*, IV., p. 282) a fatty and colloid degeneration of the muscles, which had its origin in unknown causes ; ZENKER observed the latter form of degeneration in consequence of the action of an external influence, BENNDORF (*Arch. d. Heilk.*, VI., p. 456), in consequence of freezing. COHNHEIM (*Unt. üb. d. embol. Proc.*, 1872) saw colloid degeneration of the muscles of the tongue on the second day after total ligature of that organ.

MACROSCOPICALLY, the muscles in parts deeply affected are sometimes uniformly paler, sometimes so in finely or coarsely scattered spots (at first pale reddish gray, finally brownish-yellow or whitish gray, like the flesh of fish), more homogeneous and brittle. Under the microscope the trans-

verse striation is seen to gradually disappear, and in place of them in the
unchanged sarcolemma a colorless, dull, sometimes irregularly wrinkled sub-
stance, which is broader than the normal muscular fibre, very easily broken
up transversely, always crumbling into fine fragments, and which, after a
few weeks, is gradually absorbed. The fragments of muscular fibres become
shorter, rounded, oval; between them there remains the sarcolemma as a
collapsed pouch. In rare cases the colloid substance is immediately trans-
formed into a mass of small irregularly rounded particles, which usually in
large numbers lying in contact completely fill the sarcolemma-pouch. Or,
there occurs a breaking up into thin disks (discoid division), or a " fibrillar
division."

The CONSEQUENCES of colloid degeneration of the muscles are : especially
ruptures and hæmorrhages, which occur oftenest in the lower part of the
rectus abdominis, rarely in other muscles, and sometimes smaller ecchy-
moses, sometimes circumscribed hæmorrhagic infiltrations, sometimes true
hæmorrhagic foci. The more extended hæmorrhages lead to cyst-formation
and cicatrization, or to pigmentation or liquifaction. Suppuration of
muscles rarely appears in consequence of colloid degeneration. In most
cases the degenerated muscle-fibres are entirely regenerated.

While the muscular degeneration just described is, according to ZENKER. HOFFMAN
and others, of a pathological nature, it is, according to BOWMAN, WALDEYER. ERB.
NEUMANN, found also under other circumstances. According to those last-named,
it occurs in all healthy muscles, as soon as they are wounded, and is the conse-
quence of a process similar to *post mortem* rigidity or identical with it. Also, there
appears a similar change in many pathologically degenerated muscles after death in
uninjured fibres : it then is a phenomenon of death.

A similar colloid metamorphosis of normal and hypertrophic smooth muscle-fibres
of the stomach is described by R. MAIER (*Lehrb. d. allg. path. Anat.*, 1871, p. 169).

(Waxy degeneration. ZENKER'S muscular degeneration.)

BOWMAN, *Phil. Transact.*, 1841. I., p. 69.—VIRCHOW. *Arch.*, 1852, IV., p. 266.—
ZENKER, *Ber. d. Dresd. naturf. Ges.*, 1861 ; *Ueb. d. Veränd. d. willk. Muskeln im
Typh. abdom.*, 1864.—WALDEYER, *Virch. Arch.*, XXXIV., p. 473.—O. WEBER, *Ib.*,
XXXIX., p. 216.—ERB, *Ib.*, XLIII., p. 108.—NEUMANN, *Arch. d. Heilk.*, IX.,
p. 364.

g. MUCOUS METAMORPHOSIS.

(Consult the text-books on physiology, Colloid metamorphosis, and the so-called
Gelatinous cancer.)

The substance formed by pathological mucous metamorphosis is, on the
whole, the same as physiological mucus, and has, apart from the reaction by
acetic acid, whereby it becomes coagulated in shreds, also many properties
of fluid colloid.

Mucous metamorphosis affects cells, and non-cellular substances.

1. MUCOUS METAMORPHOSIS OF CELLS

Is found oftenest in epithelia of mucous membranes and their glands, which
in great numbers show mucous metamorphosis in increased degree and in a
quicker manner. This is for the most part possible only by the quicker
new-formation of cells destroyed by the metamorphosis. This occurs on
all mucous membranes in consequence of the action of strong irritants, as
well in the state of the so-called acute or chronic catarrh, with dilatation
of the vessels affected always at the same time present. The limit between

normal and increased formation of mucus is in many places not to be drawn ; thus, especially in the mucous membrane of the nose, mouth, throat, air-passages and vagina. In the empty stomach, the surface is uniformly covered with a layer of very tough, neutral or alkaline mucus. The histological processes of mucous metamorphosis are the same as under physiological conditions ; until now it is not known whether the affected cells are destroyed by mucous metamorphosis, or whether they can evacuate the mucus without bursting.

Cells which have suffered mucous degeneration pathologically, show essentially the same character as the so much discussed CUPPED CELLS of various mucous membranes. The latter are regarded by many as artificial productions (?), while others regard them as a special kind of cell, still others as common epithelia, which have been affected by mucous metamorphosis. Pathological experience makes the latter most probable : the metamorphosis is found most often in single or poly-laminated cylindrical, and ciliated epithelia, rarely in others.

The relations which physiologists have found to exist between formation of mucus and nerve-influence are of great interest, but heretofore have been of no practical value. According to HEIDENHAIN (*Stud. d. phys. Inst. zu Breslau*, 1868, IV., p. 1) the changes which the submaxillary gland of the dog, whose secretion is extraordinarily rich in mucus, suffers by continuous irritation of the chorda tympani, consist in this, that in place of bright cells already metamorphosed into mucus, vigorous protoplasm-cells appear, so that a gland which has been cut out and examined after continuous irritation, no longer shows clear bright mucus cells. HEIDENHAIN and EPSTEIN have also demonstrated important differences in the (peptic and) mucous glands of the stomach, according as they were during hunger or in activity (during digestion). In the latter state the cells are greatly clouded, probably much richer in albumen, and give off substances into the cavity of the stomach. During hunger they are shrivelled, etc.

Consult also ENGELMANN's interesting investigations (*Arch. f. d. ges. Phys.*, 1872, V., p. 498) concerning the cutaneous glands of the frog.

Mucous metamorphosis occurs also in cells of new-formations, especially in enchondromata, in so-called mucous cysts, in cylindroma, and cancer (so-called gelatinous cancer).

2. MUCOUS METAMORPHOSIS, OR MUCOUS SOFTENING OF NON-CELLULAR ELEMENTS.

This consists in the transformation of collagen (glutin) and chondrogen into mucus or mucin, which is distinguished from the albuminates by containing less carbon and nitrogen, as well as by the absence of sulphur.

This metamorphosis affects the basis substance of cartilage, bones and connective tissue, coagulated fibrin of bloody extravasations and exudations. The cells of the first-mentioned forms are thereby either destroyed, or they persist, or exhibit processes of division. These processes are found especially often in cartilage, as well as in its periphery in articular cartilage, whereby disintegration and final lessening of the articular facets (so-called *malum senile*), as in its centre (costal cartilages), giving rise to cyst-like spaces. These softenings occur more rarely in bones with simultaneous or previous separation of lime-salts (thus in osteomalacia, in the vicinity of new-formations). In connective tissue a mucous softening appears oftenest in inflammation and in new-formations : under a more or less quick immigration or new-formation of small cell elements, the connective-tissue basis substance softens, and is either absorbed or separated or returns to its fibrous structure. Softening occurs in fatty tissue oftenest in atrophy, *e.g.*, in sub-serous fatty tissue, in yellow bone-marrow.

This mucous softening exists normally as a senile process in symphyses, and in inter-articular cartilages.

h. ŒDEMATOUS, OR SEROUS INFILTRATION.

Serous infiltration occurs in cells, and in non-cellular substances.

Serous infiltration of cells consists in the filling of them with a serous or sero-mucous substance, and in a consequent for the most part considerable enlargement. The infiltration is found from the beginning uniformly extended throughout the whole cell-substance (rarely at first in form of circumscribed drop-like spaces), so that the corpuscular protoplasm-molecules are still present at the beginning, but are separated from one another by larger intermediate spaces; later they are no longer visible. The cell has thereby become strikingly bright. Herein the nucleus remains a long time intact or enlarges only moderately; the cell-membrane (true or apparent) always becomes more distended, thinned, and then ruptures or disappears entirely without visible injury. Thereby the contents of cells lying adjacent flow together, so that finally there is formed a vesicular-shaped cavity. This is the origin of many vesicles of the skin (herpes, eczema, in part also variola), as well as of mucous membranes with laminated pavement epithelium. The same metamorphosis occurs also in the endothelia of serous membranes and lymphatic vessels.

The same peculiar swelling-up of the cells of the rete Malpighii is found in blisters from vesication and pemphigus. These are rounded, their protoplasm is quite homogeneous, dull, but seems to show in parts canalicular pores; the for the most part diminished, rounded or angular nucleus lies in a proportionately large cavity, filled probably with serous fluid. (*Vide* VOIGT, *Arch. d. Heilk.*, X., p. 420.)

That the contents of the affected cells are serous in character, is shown by micro-chemical reactions. That the metamorphosis does not owe its origin to a simple mechanical taking up of serum from out of the vessels of the subjacent mucous membrane, but to a real cell-activity, is shown by its sharp limitation in many parts of the skin and mucous membrane.

RANVIER (*Nouv dict.*, etc.) describes as a pathological change of laminated flat epithelium a dilatation of the corpuscular nucleus. This is transformed into a translucent, slightly refractive vesicle, which continuously enlarges to bursting. At first the nucleus resembles a half-moon; later it is destroyed. The cell ceases to develop and dies. This change is found in all inflammatory cutaneous affections, in the neighborhood of wounds, ulcerations, tumors, in erythema, erysipelas, eczema, in the erythematous zone of small-pox, etc. It causes desquamation. R. found the same in mucous membranes.

Slight degrees of metamorphosis may return to the normal state; in higher grades it results in destruction of cells.

Whether O. WEBER's dropsical degeneration agrees with the results obtained by myself, cannot with certainty be inferred from his description. (*Hdb. d. Chir.*, 1865, p. 330.) He places it in histological relation with mucous metamorphosis. It occurs in granulation-cells and pus-corpuscles in the permanent water-bath, in cells of all kinds in œdematous saturation of tissues, on the inner surface of many cysts.

Serous infiltration of non-cellular substances is known only in few places, but not accurately: in the so-called membrana propria of mucous and serous membranes, in the tunica propria of the urinary tubuli—in many inflammatory states of these parts.

A peculiar œdema of the albuminous substances, of cell-contents, as well as of the basis substance of the cortex of the brain, is either in consequence of the addition of water to microscopical preparations of normal brain substance, or a sign of increased water in the brain itself (HUBRICH, *Ztschr. f. Biol.*, 1866, II., p. 391. BUHL, *Ib.*, p. 396).

MARTINI (*Med. Ctrlbl.*, 1871, No. 41) describes a so-called "serous atrophy" of primitive muscle-bundles occurring in sarcomata, lipomatosis, etc. It consists in this, that rounded or oval openings are filled with serous fluid, and coalesce by the disappearance of the surrounding transversely striated substance.

Concerning serous infiltration of connective tissue, etc., see Œdema, p. 225.

Under the microscope, bright spots are not infrequently found in single, otherwise normal cells of the most varying kinds, with respect to which it is difficult to distinguish whether they are artificial (by the addition of liquid in the process of preparation), or the result of disease. In the latter case it must often remain doubtful, whether the spots are of a serous, or mucous, or colloid character.

In the moist chamber, epithelial cells are seen to become hyaline and blend with neighboring cells into large masses. The structure again appears by acetic acid. Absolutely hyaline, soft jelly-like masses of very varying size are found between the epithelial cells in the cornea of a frog, if it has been twenty-four hours previously touched with common acetic acid. They not infrequently contain migratory cells. They are probably transudations. In pleuritic effusions colossal gelatinous masses are found, in blisters from vesication gelatinous fluid. The influence of air is very favorable to coagulation. (F. A. HOFFMANN, *Virch. Arch.*, LI., p. 373.)

i. CROUPOUS METAMORPHOSIS.

E. WAGNER, *Arch. d. Heilk.*, VII., p. 481; VIII., p. 449.—Vide p. 263.

Croupous metamorphosis consists in the transformation of cellular contents into a substance externally similar to coagulated fibrin. It occurs on mucous membranes of every kind (as so-called croupous and diphtheritic exudation, especially of the larynx, trachea and pharynx), perhaps also in some glandular organs (especially in the urinary tubuli, as so-called hyaline or fibrin cylinder, and in the lungs, as so-called croupous pneumonia).

Concerning the more immediate histological relations, see p. 264.

Besides, this metamorphosis occurs also as a chronic process, especially in the kidneys.

The common urinary cylinder, and THOMAS' cylindroid, have the general reactions of protein bodies, but agree with none of them exactly.

Concerning the so-called urinary casts having their origin partly in this, partly in colloid metamorphosis, see AXEL KEY, *Med. Arch.*, I., p. 1, *Stockholm*, 1863, and O. BAYER, *Arch. d. Heilk.*, 1868, IX., p. 136.

SLAVJANSKY (*Ber. d. k. s. Ges. d. Wiss.*, 2. Nov. 1872) has described a like histological change, as so-called reticular degeneration of the serous envelope of the ovum of the rabbit.

COMBINATIONS OF TWO OR MORE METAMORPHOSES.

Combinations of two or more metamorphoses occur not infrequently. They occur in the same organ independently of one another (*e.g.*, pigment-infiltration and calcification); or, with one another and from like causes (as fatty and chalky degeneration of the arteries); or, one degeneration is the cause of the other (*e.g.*, fatty metamorphosis of renal epithelium with lardaceous degeneration of the vessels); or, finally, two metamorphoses

occur at the same time (as fatty and mucous degeneration, colloid degeneration and calcification, pigmentation and fatty metamorphosis).

Two kinds of combinations are especially conspicuous: pseudo-croupous inflammation of mucous membranes, and atheromatous process in arteries.

Pseudo-croupous inflammation of mucous membranes consists in manifold changes of the epithelia and in inflammation of them, or at the same time with that of the tissue of the membrane. The changes are: albuminous infiltration, for the most part with simultaneous fatty metamorphosis of moderate extent, for the most part greatly increased formation of mucus by the mucous membrane itself and its glands, new-formations of epithelium (processes of division—pus-formation). To these belong also the products of inflammation of the epithelium and of the tissue of the mucous membrane: serous exudation, pus-corpuscles, often red corpuscles, and for the most part, numerous fungi of the lowest forms. Macroscopically, the mucous membrane is shown to be covered with a cloudy (lighter or darker, according to the quantity of escaped blood), mucous, sometimes viscous substance, under which lie the changed, variously formed, unadherent epithelia. In parts, there are deeper losses of substance, for the most part to the deepest epithelium. These inflammations are found best marked in the mucous membrane of the mouth, throat and air-passages in variola, in the mucous membrane of the intestine, in many cases of primary and secondary dysentery.

The ATHEROMATOUS PROCESS consists in a combination of inflammatory or other softening with fatty, also not infrequently with chalky metamorphosis. Softening affects mostly basis substances, fatty metamorphosis affects mostly the cellular elements. The process occurs only in connective-tissue substances, most often in the internal coat of large arteries. On the surface of these it forms the so-called ATHEROMATOUS ULCER, deeper in the atheromatous focus. Both contain so-called atheromatous mortar, i.e., parts in fatty, in part also chalky degeneration, especially cells, particles of softened basis substance, and mostly cholesterin.

2. GANGRENE.

(NECROSIS, MORTIFICATION, SPHACELUS OR COLD GANGRENE, WARM GANGRENE, MUMMIFICATION OR DRY GANGRENE, etc.).

FABR. HILDANUS, De gangræna et sphacelo, 1593 and 1646.—QUESNAY, Traité de la gangrène, 1750.—O'HALLORAN, On Gangrene and Sphacelus, 1765.—KIRNLAND. On Gangrene, 1786.—HALLER, Ueb. d Fäulniss lebender u. todter thierischer Körper, 1793.—WHITE, Bemerk. über den kalten Brand. Transl. by WICHMANN, 1799.—HIMLY, Ueb. d. Brand. d. weichen u. harten Theile, 1800.—NEUMANN, Abh. v. d. Brande, 1801.—DELPECH, Mém. sur la compl. des plaies et des ulcères comme sur le nom de pourriture d'hôpital, 1815.—GASPARD, Journ. de phys., 1822. II., p. 1, and 1824, IV., p. 1.—V. FRANÇOIS, Essai sur la gangrène spontanée, 1829.—CARSWELL, Art. Mortification in Ill. of the Elem. Forms of Dis., 1834.—HECKER, Unters. üb. d. brand. Zerstör. durch Behind. d. Circul., 1841.—OSCHWALD, Ueb. d. Brand., 1847. —PITHA, Prag. Vjschr., 1851, II., p. 27.—VIRCHOW, Würzb. Verh., I., III.; Arch., I., p. 272, V., p. 275; Wien. Wochenschr., 1851; Handb. d. spec. Path. u. Ther., I., p. 278; Verh. der Berl. med. Ges., 1865, I.—HARTMANN, Virch. Arch., 1855, VIII., p. 114.—DEMME, Ueb. d. Veränderungen der Gewebe durch Brand., 1857.—KUSSMAUL, Virch. Arch., 1858, XIII., p. 289.—BRYK, Ib., 1860, XVIII., p. 377.—RAYNAUD, De l'asphyxie locale et de la gangrène symétrique des extrémités, 1862.—O. WEBER, Hdb. d. Chir., 1865, I., pp. 106 and 548.—SAMUEL, Virch. Arch., LI., pp. 41, and 178; LIII., p. 552.

(Consult besides the literature of Embolism, and of Inflammation.)

GANGRENE, NECROSIS, MORTIFICATION is the absolute cessation of life, especially of the circulation of the blood and juices, and consequently of nutrition, also of the warmth, sensation, motion, and function of a part of the organism. If at the same time putrefaction, a development of stinking gases, occurs, the process receives the name of GANGRENE, or SPHACELUS.

GANGRENE (hot gangrene) is that form in which the parts, before the appearance of complete gangrene, are still hot and painful, and acutely inflamed.

Besides, there are special terms applied to gangrene of different organs or tissues: NECROSIS is commonly used for gangrene of the bones, as well as of cartilage; PHAGEDÆNA is commonly applied to gangrenous destruction of ulcers. As CARIES SICCA of the teeth (in opposition to caries humida) are not infrequently designated processes which are of a gangrenous nature. The words CARIES and NECROSIS, applied to the bones, are often interchanged. But, in fact, there not infrequently occurs in caries (the so-called bone-ulcer) a not merely molecular, but a grosser necrosis.

The dead portion of tissue has received special names for individual textures: in the bones it is called SEQUESTRUM; in cold, hot, and phagedænic gangrene of external parts, in gangrene of typhous new-formations, etc., it is called SLOUGH.

The question, as to what affections are to be included under gangrene, it is for many difficult to determine. This holds true, in the first place, of simple atrophy (see p. 293). Also of ulceration, which many call a molecular gangrene (see p. 283). But, since in ulceration suppuration for the most part predominates, it seems advisable (in accordance with the maxim: *a potiori fit denominatio*) to place those among the inflammations. This view does not require that many ulcers, *e.g.* the so-called phagedænic, should be regarded otherwise than as belonging with greater right to gangrene. Finally, there are the so-called gangrenous inflammations (see p. 285).

Gangrenous parts act very differently, according to their structure and vascularity, according to the causes of the gangrene, its acuteness, and the possibility of an access of atmospheric air, etc. Whether a part is quickly destroyed after the appearance of gangrene, depends altogether upon its contained blood and texture. A necrotic bone preserves, in contrast with a carious bone, its smoothness and cohesion, even its general microscopic texture. But if the parts attacked by gangrene are soft, they become by gangrene still softer, while their elements lose their mutual cohesion and fall to pieces. If they contain a greater quantity of blood, the blood-corpuscles also are destroyed, their coloring matter pierces the tissues, there arises the so-called false red œdema; or there occur through imbibition of the coloring matter of the blood darker blue and black colorations.

AEBY (*Med. Ctrlbl.*, 1871, No. 14) has shown especially the reason of the unchangeableness of organic bone-substance. Fresh compact bone, taken from the dead body, contains eleven to twelve per cent. water, and a mean of twenty-eight per cent. of organic substance. Bone does not putrefy, because it cannot swell, in consequence of its inflexibility. Pulverized bone immediately experiences swelling and quick putrefaction.

The functional phenomena of paralysis, moreover, determine the external symptoms of gangrene: paralysis, insensibility, so-called marble coldness, dryness of surfaces, collapsed appearance of the part.

CAUSES OF GANGRENE.

In GENERAL, gangrene is caused either by INTERRUPTION OF THE BLOOD-SUPPLY OF NUTRITIVE MATERIAL, chiefly,—or by DESTRUCTION OF THE TISSUE

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ELEMENTS. Both may occur slowly or quickly, directly or indirectly, and so give rise to very different forms of gangrene.

SPONTANEOUS DEATH, so-called (*necrosis spontanea*), depends either upon this, that the same causes have exerted their influence, only imperceptibly and more slowly : thus inanition in the insane, which brings nutrition to a low grade, whereby an inflammation, which induces a disturbance of the tissues, so much the more easily interrupts nutrition and causes necrosis. Or there are embolic occlusion of arteries, etc.

Gangrene occurs PHYSIOLOGICALLY, as, *e.g.*, in the decay of the ligated umbilical cord, the falling out of the milk-teeth, in various parts in old age.

All parts are, in general, PREDISPOSED TO GANGRENE, in which there exists a disturbance of the circulation of any kind (anæmia, hyperæmia, thrombosis, hæmorrhage, œdema) ; but these disturbances usually induce gangrene only in their highest grades. Inflammation in all its effects, especially parenchymatous exudation and purulent infiltration, likewise disposes to gangrene. In a similar manner, probably, a faulty blood-mixture, as in inanition and diabetes, in drinkers, perhaps also in various acute and chronic forms of marasmus, caused by hunger as well as by disease (typhoid fever, etc.), leads to gangrene.

Gangrene, according to its special cause, appears sometimes in strong, well-nourished individuals, sometimes in weakly, marasmic, badly nourished persons of every age of life : in the latter, *cet. par.*, it appears more easily and is more extensive. We see the former, *e.g.*, in gangrene from embolic occlusion of arteries, in strictured part of the intestines ; the latter in scorbutus, noma, etc.

The same disposition to gangrene is found in parts of the body after interruption of nervous activity, nutrition, etc. : *e.g.*, in injury of sensory nerves, especially of the fifth (peculiar corneal softening), in parts paralyzed as to motion,—in both cases less because insensible or immovable parts can sufficiently escape injurious external influences (in paralysis, moreover, because the support to the venous blood-circulation is destroyed), than on account of the simultaneous paralysis of the vaso-motor nerves. Also, dropsical parts (extremities, scrotum, external female genitals : so-called white gangrene) are disposed to gangrene, and to a less degree frozen extremities.

Gangrene appears more early, *ceteris paribus*, under the thick skin (*e.g.*, of the neck and back), under fasciæ, than in other parts : *e.g.*, of carbuncle of the neck and back, the so-called phlegmonous inflammations, deep paronychia, penetrating wounds of the fasciæ.

According to SENFTLEBEN (*Virch. Arch.*, XXI., p. 289), the localization of necrosis depends chiefly upon the histological character of the periosteum of different parts. In the humerus, necrosis occurs especially in the vicinity of the tuberosities, and parts corresponding to the insertion of the deltoid and pectoralis major ; in the ulna, in the coronoid process ; in the radius, in the vicinity of the tuberosity ; in the pelvis, in the tuber ischii ; in the femur, in the trochanter major, and in the internal and posterior part of the bone corresponding to the point of attachment of the adductor magnus ; in the tibia, anteriorly and internally.

The SPECIAL CAUSES OF GANGRENE are :

1. INTERRUPTIONS IN THE SUPPLY OF NUTRITIVE MATERIAL.

Arrest of the blood-circulation does not alone necessarily and immediately lead to gangrene, provided new nutritive and exudation fluid is supplied

from the vicinity of the parts deprived of circulation. Gangrene appears, however, if the circulation of the juices has become impossible, if the tissue itself has become impassable for nutritive fluid, for the fluid of the tissue, and for the intermediate current of juices.

Tissues which have been deprived of a circulation pathologically, like those similarly deprived physiologically, become seats of inflammation. Where the permeability of the parenchyma is destroyed by burning, drying, destruction, by the most various chemical metamorphoses, there gangrene is inevitable. Most cases of gangrene depend upon the SIMULTANEOUS impermeability of the vessels and of the parenchyma. (SAMUEL.)

a. Severe disturbances of the blood-supply are found most strikingly in OCCLUSION OF ARTERIES (naturally with the exception of that of the functional pulmonary artery), to whose regions no blood or not a sufficient quantity can enter by collateral branches. This takes place in consequence of coagula, which have a local origin (in chronic endarteritis, fatty degeneration and calcification of the muscular coat)—so-called THROMBOTIC NECROSIS; or which are so-called emboli (thus, for example, gangrene of the left lower extremity, softening of the brain, perhaps also the round gastric ulcer, etc., in diseases of the heart)—so-called EMBOLIC NECROSIS. The embolus lies sometimes near the gangrenous spot, sometimes is far from it, e.g., in the popliteal space, in gangrene of the toes.

High degrees of chronic arteritis, especially of the smaller arteries of the lower extremities, are likewise followed, alone or simultaneously, with fibrous or fatty degeneration of the heart, by gangrene (gangræna senilis). That both forms of gangrene, embolic as well as that dependent upon chronic arteritis, affect the lower oftener than the upper extremities, depends in the case of embolism upon the comparatively rectilinear course of the vessels from the heart to the femoral arteries; in that of chronic arteritis, upon the feebleness of the current increasing with the distance from the heart.

By ligation of the cœliac artery the gastric mucous membrane is in some parts insufficiently nourished, and therefore becomes necrotic; the production of acids does not cease, but, on the contrary, by the diminished alkalization on the part of the circulating blood it is increased, and thus there results a self-digestion, or a so-called GASTRIC ULCER. (COHN, Klin. d. embol. Gefässkrkh., p. 515.)

According to ESTLANDER (Arch. f. klin. Chir., 1870, XII., p. 453), gangrene in the lower extremities in typhus fever arises from thrombi, which are formed during the weakened condition of the heart, in the left ventricle, and with its increasing strength are carried as emboli into the arteries of the extremities.

Many cases of pulmonary gangrene in cancer of the œsophagus proceed perhaps from compression of the bronchial arteries.

BUHL (Lungenentz, etc., 1872, p. 77) describes the origin of true acute pulmonary caverns (distinguished from the more frequent bronchial caverns) from the, by him so-called, desquamative pneumonia: if the cell and nuclear growth in the arterial sheath be so considerable that nutrition is suspended, the dead mass will be separated by limiting suppuration.

SPIEGELBERG and WALDEYER (Med. Ctrlbl., 1867, No. 39; Virch. Arch., 1868, XLIV., p. 69) found in bitches, in whom a portion of the uterus had been extirpated, no retrograde, especially no gangrenous degeneration, in the constricted portion separated by the ligature; connections were found to exist with the attached meso-uterine folds of the peritoneum and the remaining portion of the uterus; numerous vascular connections were supplied to both portions.

The same conditions exist in affections of the bones and cartilages, through the accumulation and pressure of blood and pus under the (vessel-bearing) periosteum or perichondrium; in the skin after traumatic separations of the subcutaneous connective tissue; in the skin and fasciæ of the extremities

and vertex of the cranium in so-called phlegmonous, or pseudo erysipelatous inflammations.

Other forms of occlusion of arteries, as by ligature, etc., by nervous influence (spastico-ischæmic gangrene), are attended by the same results, unless there is formed a sufficient collateral circulation.

Gangrene after the long use of ergot, as well as the so-called symmetrical gangrene of RAYNAUD, is, according to many, a consequence of spastic ischæmia of the smallest arteries. According to ESTLANDER (l. c.), the stases, petechiæ, etc., in typhus fever are dependent upon spastic anæmia of the small and smallest arteries, dependent upon poisoned blood. This lasts a long time, and the finer veins are filled through the collateral branches, thus giving rise to a bluish color.

RAYNAUD'S SYMMETRICAL GANGRENE occurs chiefly in chlorotic and nervous individuals, rarely in children and older persons, perhaps also in typhoid fever, etc. It most frequently attacks the fingers, rarely the toes, tip of the nose and external ear. Often for months beforehand the affected parts suddenly become white, bloodless, without feeling, dead ; the skin is strongly wrinkled and shrunken, the ends of the fingers appear thin and conical. The temperature of the parts is sunken, they appear without feeling, and the muscular movement is as though paralyzed. If this state extends itself over a whole extremity, the pulse becomes imperceptible. After a variously long time there follows a painful reaction : itching arises and the feeling of over-filling of blood, the skin becomes bluish-red. Severe pains precede the proper outbreak of gangrene. The extremities become bluish-white, violet, dark, livid, marbled ; they are insensible, but very painful and icy cold ; then small vesicles appear, which fill with sero-purulent liquid and are usually destroyed, so that the cutis becomes laid bare. Even now the part may be restored. But, for the most part, after some time the attack returns, and then the fingers show numerous small, white, depressed and hard cicatrices on their extremities, which are found specially in front of and beneath the nails, and form conical callosities. If the ischæmia is of longer duration, there follows from the consecutive hyperæmia a true mummification, which terminates with the falling off of a part of the last phalanx.

b. Gangrene rarely proceeds from the VEINS, because of their manifold communications, and then only when all the veins of a part are compressed or obstructed, and when, in consequence of this, there results overfilling of the capillaries, and hæmorrhagic infiltrations. This does not occur in simple thrombosis, therefore here gangrene never appears ; but indeed during compression, when all the venous branches pass through foramina, narrow channels (herniæ, invaginations—prolapse of polypi and hæmorrhoidal tumors) ; also in high degrees of paraphimosis ; in transplanted pieces of skin, whose veins become impervious by being pulled or twisted. Light bandages, ligatures, etc., may have the same result. Gangrene behaves also in essentially the same manner, which is the result of slowly formed arterial embolism, which first gives rise to venous hyperæmia, etc.

In many cases of senile gangrene of the toes, the essential cause is a marasmic thrombosis of the small veins, and the diminished nourishment of parts dependent upon them. In thrombosis of the gastric veins and vena portæ, there arises a high degree of venous hyperæmia of the affected parts, and, in consequence of it, hæmorrhagic infiltration, and the so-called round gastric ulcer (L. MÜLLER).

While many regard the cause of the round gastric ulcer to be spastic contraction of the smallest arteries, its cause, according to AXEL KEY (*Hyg.*, 1870, p. 261 ; *Nord. med. Ark.*, 1871, III., 1, No. 5), resides in the strong contractions of the muscular coat with spasm in localities, so that the venous circulation in these places is suddenly more or less completely arrested.

c. Gangrene has its origin in various ways in the CAPILLARIES: 1, through complete anæmia of the part in consequence of external or internal pressure ; 2, through complete interruption of the blood-current (so-called

stasis); 3, through infiltration of tissues with fibrin, extravasated blood, pus, and chiefly with new-formations; 4, through high degree of fatty metamorphosis of connective-tissue corpuscles.

Gangrene from anæmia in consequence of external pressure, arises sometimes from bandages, from continued rest on hard parts (sacrum, trochanters, etc.), especially in states of general weakness. In like manner a pressure may act from within outward. Thus the skin or mucous membrane over large and quickly growing abscesses, aneurisms or other form of tumor is changed, in consequence of high degree of anæmia from pressure, into a whitish or yellowish slough, after the throwing off of which there appears for the most part a gangrenous ulcer.

If the quantity of the circulating blood is too small in proportion to the parts to be nourished, as, for example, in cancerous new-formations, and the acid gastric juice acts upon these as in the stomach, they become changed into a sometimes altogether peculiar manner : they become soft, colored gray or grayish brown, but they are odorless.

Gangrene from complete arrest of the blood, or from stasis, appears only then, when the arrest of the blood lasts and the blood is not again set free. It affects capillary districts of various size, besides the smallest arteries and veins. (Stasis of larger vascular districts belongs to thrombosis.) The causes of stasis are in part purely mechanical (wounds of soft parts, as in every border of wounds ; high degrees of arterial ischæmia and venous hyperæmia) ; in part physico-chemical (cold, warmth ; chemical substances : so-called stasis of diffusion).

The phenomena and causes of stasis, which in transparent parts of cold-blooded animals have been so often investigated, were for a long time regarded as a chief event of inflammation, or (EMMERT, HENLE) as identical with inflammation. After that BRÜCKE and H. WEBER had established the mechanical and chemical conditions, first the English observers, and then VIRCHOW showed that these experiments could not be applied to man and warm-blooded animals without reserve, and that complete stasis must always lead to necrosis and ulceration. O. WEBER has lately again made conspicuous the importance of stasis, especially of that arising from diffusion, and has more nearly decided its relation to inflammation and gangrene.

That a greater part of the stases arising through the application of chemical substances (acids, alkalies, salts, etc.) to transparent animal parts depends only upon processes of diffusion, is shown by the experiments of SCHULER : if the concentration of the blood of the frog is increased or diminished by injection of water or solutions of salt into the veins, greater stasis appears, the more the density of the blood is diminished by the liquid from without acting as an irritant, while it results so much the more slowly when the per cent. of solution approaches that of the fluid within the vessels. The greater the diffusibility of a substance, the more marked and energetic is the stasis caused by it (corrosive substances). Besides, the degree of concentration, the nature of the substance, and its chemical relation to the blood and blood-serum are also of the greatest influence. According to O. WEBER, stasis, during the operation of high degrees of heat, especially of a glowing heat, is chiefly dependent upon the immediate thickening of the blood. A quick evaporation operates also in the same manner (EMMERT).

Of importance in the production of stasis, besides diffusion, are also the blood-pressure, the physical and chemical character of the blood as well as of the fluids of the tissues, the varying porosity of the vessel-walls, as well as the diameter of the afferent and efferent vessels. Quick necrotic destruction of the brain after wounds of the skull, perforating wounds of the abdomen, connected or not with prolapsus of the viscera, and killing quickly by gangrene without proper peritonitis, the necroses of exposed ends of bones, do not depend upon the exposing of the neighboring membrane, but upon stases developing quickly and in great extent under the influence of unusual evaporation (O. WEBER).

Gangrene occurs but rarely from infiltration of tissues with fibrinous

or albuminous molecules, while in most cases of so-called diphtheritis, or phlegmons, as well as of dysentery, other changes are almost always present (hyperæmia, hæmorrhage, suppuration). Likewise, gangrene from hæmorrhagic infiltration is rare, while the cases so regarded are partly hæmorrhages with extended laceration or bruising of the tissues, partly traumatic inflammations, partly hæmorrhagico-inflammatory infiltrations (e.g., anthrax). Gangrene from dense infiltration with nuclei and cells, narrowing or closing the capillaries, occurs in many suppurations (many so-called diphtheritic, better-named forms of phlegmonous inflammation of the throat, intestines, uterus, etc.), in tubercle (so-called yellow tubercle), in typhous new-formations (sloughs of typhoid fever), in the exudation of cerebro-spinal meningitis, in catarrh of the nasal mucous membrane, etc. : thus under circumstances where the collateral circulation is insufficient, or where no new vessels have been formed.

BUHL proposes for such cases, instead of the terms diphtheritic inflammation, or diphtheritic exudation, the names : acute sloughing, acute tissue-necrosis, necrotic exudation. He urges rightly, that the growth of free nuclei surpasses the number of cells, that the nuclei are round, oval, pear-shaped, etc., with sharply defined contour.
In many cases referred to in this category (mykosis of the stomach and intestine) bacterian formation is the first condition, followed by a high grade of hyperæmia and hæmorrhagic infiltration, and gangrene.

Gangrene from high degree of fatty metamorphosis of connective-tissue corpuscles rarely occurs of itself, oftener with hæmorrhages and inflammations. The corpuscles mentioned are quickly filled with fat-molecules, are destroyed, and therewith the nutrition of the whole tissue fails, so that necrosis appears.
Here especially is to be referred gangrene from inflammation in parts which are completely or incompletely paralyzed, gangrene in inflamed dropsical parts, probably also the so-called noma of the face and genitals in cachectic individuals.

HIRSCHBERG (Berl. klin. Wochenschr., 1868, No. 31 and 32) describes an ulceration of the cornea in little children, dependent upon encephalitis, which ulceration is of a neuro-paralytic character, and with which children from two to six months old die from digestive troubles and marasmus, but usually without pronounced brain-symptoms.
In many cases, where gangrene proceeds originally from the capillary vessels, a venous, more rarely arterial thrombosis appears SECONDARILY. To distinguish them from primary, i.e., embolic thromboses, is sometimes very difficult. This is most often the case in senile or marasmic gangrene.

Gangrene never results from diminished activity of the heart alone in acute or in chronic diseases (typhoid fever, pyæmia, acute exanthemata—chronic cachexiæ of every kind) ; only with simultaneous changes in the arteries, or extended thromboses (gangræna senilis), or continuous pressure upon the part (bed-sore

A more disputed point has always been the relation of arterial obstruction and the changes of the heart's muscle to gangrene. The artery is found filled sometimes with coagula, sometimes it is found empty. The coagula are sometimes secondary to the gangrene, sometimes they existed before and are the causes of gangrene. MUMMIFICATION, dry gangrene of the extremities, is always the consequence of imported coagula, of emboli. The so-called spontaneous gangrene in rheumatism with endocarditis has for the most part this foundation. Other forms of so-called spontaneous gangrene, as it often occurs, for example, in old persons (gangræna

senilis) are connected with arterial disease, but the nearest arteries are usually found free from coagula, at least from old ones. Disease of the arteries and of the heart's muscle impedes the blood-current, especially in most distant parts, as the feet. Light frictions, pressure, slight inflammations, cold determine, more quickly an outbreak of necrosis, than in normal nutrition. In a similar manner also is *gangræna ex decubitu* produced, which has its origin neither in obstruction of arteries nor in inflammation. The enfeebling force lies here in the torpidity, or true fatty degeneration of the heart, as it appears in consequence of all severe diseases (especially severe typhus and typhoid fevers, pyæmia, spinal paralyses). The sore follows in consequence of continued pressure : so-called NECROSIS OF COMPRESSION. It is found especially on the sacrum and trochanters, rarely on the heels, spinous processes of the vertebral column, scapula, head of the fibula, the back part of the head, wherever the hard bony supports increase the pressure.

The duodenal ulcers often found after severe burns, freezing, more rarely from alcoholic abuse, are, according to FALK, consequences in part of depressed heart's action, in part of the corrosive action of the intestinal contents.

2. GANGRENE FROM DISORGANIZATION OF TISSUE-ELEMENTS.

The causes in question give rise in their slightest grades only to congestive hyperæmia, in their higher grades to inflammation, in their highest grades to gangrene ; these three processes sometimes pass in a single case into one another.

a. A disorganization of tissues occurs after SEVERE WOUNDS of every kind (stabs, shots, etc.), but especially after bruises, when they result in complete destruction, in external parts of every form : so-called gangrene of destruction, *gangrène foudroyante ;* as well as in internal parts, oftenest in the cervix uteri, vagina and vulva after severe births, but also in the brain and lungs, without or with simultaneous injury of the surrounding soft and bony parts.

b. After CONCUSSION (brain, bones) a somewhat similar thing probably occurs, but the anatomical relations are still undecided.

c. FREEZING and BURNS, in their higher grades, are attended directly by the same results ; indirectly, they act, in their lower grades, by producing anæmia or venous hyperæmia.

The ear of a rabbit can be rendered stiff, hard and immovable by a continuous spray of sulphuric ether. The blood-column becomes fixed and immovable. After a few minutes the ear becomes soft, flabby, as if soaked with water, the blood fluid and easily movable. For the most part, in the course of from one-half to one hour, there appears the form of an acute inflammation. (SAMUEL.)

According to RICHARDSON (*Med. Times and Gazette*, May, 1867), the brain and spinal cord, besides the medulla oblongata, of frogs, rabbits and doves can be frozen : after these organs have been thawed out, their functions are completely restored. R. could freeze and thaw again the brains of doves over forty times, without detriment to the comfort and intelligence of the animals, and hold them for five hours in the frozen state.

SAMUEL (*Med. Ctrlbl.*, 1869, p. 306), in his experiments by scalding the ears of rabbits, whose carotids had previously been ligated, found that with a scalding heat of 62 C. the anæmic ear became gangrenous without having suffered previous inflammation, while in the uninjured ear of a like strong rabbit regular suppurative inflammation was developed.

d. CHEMICAL SUBSTANCES (concentrated acids and alkalies—corrosive substances chiefly) act either by withdrawing the watery constituents from the tissues, or by entering into chemical combinations with the tissue-elements. Their action has been observed, in part accidentally after poisoning, etc., in part during their use therapeutically.

The changes arising from the action of corrosive substances have been, with respect

to the chlorides, most thoroughly studied by BRYK (l.c.). Inflammations from cor-
rosive substances are characterized in the first place by the presence of sloughs,
then by blood-coagula in the immediately adjacent vessels, which extend into the
capillaries. The slough contains mostly mummified, in part fatty tissue: accordingly,
the slough is generally dry and hard, as by concentrated metallic chlorides; or
soft and liquefying, dependent upon greater and quicker fatty metamorphosis, as
by chlorine, chlorides of the alkalies, and dilute solutions of metallic chlorides.
Between the gradually shrunken slough and the remaining free parts, there is a
layer of fatty degenerated tissue; by the destruction of which the loosening of the
slough is accomplished. Now the so-called reactive inflammation begins in the pre-
served tissue: first as nuclear growth in the connective tissue of the skin, 6–8 hours
after the beginning of the effect of the caustic, likewise nuclear increase and
sprouting on the capillaries. The fatty layer between the slough and tissues is
resolved into a cheesy pulp. The slough loosens. On the fourth or fifth day, more
serum exudes from out of the granulation layer, and pus is formed, which washes
away the débris of the tissues. Suppuration and cicatrization follow. Nuclear
growth and suppuration are now much less than before, because thromboses are
numerous and extend into the capillaries; at the same time also on account of the
pressure of the appearing slough. On the tenth or twelfth day, when the slough
falls off entirely, cicatrization progresses. Fever is entirely absent or is moderate.
The urine is often increased, contains much epithelium belonging to the urinary
tubuli, and albumen. The epithelium is often granular and clouded by the metallic
chlorides. The urinary changes disappear on the third to the fifth day after cauteri-
zation, when the slough is disconnected from the vascular tract.
  The so-called SOFTENING OF THE STOMACH does not belong to this class: it
appears first after the appearance of death and only then, when the contents of the
stomach passes into strongly acid fermentation. W. MAYER (D. Arch. f. klin. Med.,
1871, IX., p. 105) describes a case of gastro-malacia before death.
  According to KUSSMAUL'S experiments, chloroform also must be included here.
If it be injected into the arteries of dead animals, putrefaction is prevented, while
the same is excited by it in living animals. If the animal lives a sufficiently long
time after the injection, there will be sustained in the dead member for one or two
days a lively blood-current. This furnishes the explanation, why in living animals
the rigidity from chloroform is so quickly suspended and putrefaction appears.
Probably the chloroform is washed by the blood-current out of the limb and thus
the tissues are robbed of that material which had killed them, but at the same time of
the power it had to protect from putrefaction. Chloroform is only a mortifying, not
a septic agent. Putrefaction appears only when chloroform has been removed, and
it is the blood, which now under conditions so changed, acts contrary to its former
manner destructively on the changed tissues, whilst it furnishes the three chief
conditions for the excitation of putrefaction: warmth, oxygen and water. It bears
the same relation to gangrene or putrefaction of parts rigid by chloroform, as to
gangrene of frozen parts. Antiseptic agents, frost, and chloroform, may induce
sepsis indirectly by killing the tissues, if the parts thaw out, or the chloroform is
carried away by the blood-current.

  e. Here belong also numerous cases, in which the form of disorganization
of tissues is not wholly clear, in which the immediate cause lies either in
physical or in chemical influences, or in the presence of fungi. Physical
agents which reaching from without to, or within the body, cause some-
times only inflammation, sometimes this followed by gangrene, sometimes
the latter from the beginning. These conditions are oftenest found in the
air passages and lungs (pulmonary gangrene), if, from whatever cause,
expectoration is rendered difficult. With respect to many bodies, it is
doubtful whether their mechanical or chemical force is the cause of the
gangrene: in many gangrenous inflammations of the lungs, and of serous
membranes.
  The forms of gangrene dependent upon chemical decompositions of
known or unknown nature, are very numerous. Here belong infiltration
of tissues with secretions and excretions, especially urine, and the excre-
ment; putrefactive decompositions (so-called putrescence) of ulcerous sur-
faces and wounds, as they occur in over-filled and badly ventilated sick-

rooms, with deficient cleanliness, in moist warm air, or by foreign bodies on the external skin and bordering mucous membranes, especially on the internal surface of the puerperal uterus. Putrid bronchitis during severe diseases of the mouth and throat is explained by decaying blood and secretions of wounds (in operations), by putrefactive processes (diphtheritis, ichorous cancers of the tongue, etc.); the same disease and pulmonary gangrene are explained in those severely sick, and in the insane in part by particles of food, which, accidentally or during artificial nutrition, find their way into the bronchi and there become putrid. In like manner do large bodies, which have found their way into the bronchi, especially organic matters (bones), not infrequently cause gangrenous pneumoniæ. The secretions remaining on the ulcerated mucous membrane of the nose, ear, in bronchiectases, oftenest those of the lochiæ on the mucous membrane of the uterus cause putrescence of the mucous surfaces. Also ichorous ulcers, especially cancers, which perforate the parenchyma, and often cause gangrene of the latter (e.g., pulmonary gangrene from cancer of the œsophagus). Even long-lasting uncleanliness from urine or excrement may cause inflammation and gangrene. Thrombi, which are impregnated with putrid substances, if they become embolic, induce like decompositions: e.g., pyæmic thrombi of various parts of the body, especially those of the cranial sinuses in diseases of the ear, perhaps also many marasmic thrombi.

Among those forms of gangrene, in which vegetable parasites are the essential causes, almost the only one generally acknowledged is gangrene of the spleen, and the carbuncle of gangrene of the spleen (see p. 103). Many here include also hospital gangrene, pyæmia with puerperal fever, malignant diphtheritis of the throat, the poison of dead bodies. The so-called putrid bronchitis, and pulmonary gangrene are with greater probability dependent upon fungi, and indeed upon micrococci and bacteria, perhaps also upon leptothrix and sarcina: these fungi cause, in the lungs as well as in external dead parts, a process of chemical decomposition.

It is not yet decided to what extent fungi are associated with the different forms of gangrene. In the greater number of cases the fungous formation is secondary. According to TRAUBE (D. Klin., 1853, p. 409; 1861, No. 50 ff; 1862, p. 41), and LEYDEN and JAFFE (Arch. f. klin. Med., 1866, II., p. 489) putrid bronchitis and many forms of pulmonary gangrene are dependent upon fungi, especially the so-called leptothrix pulmonalis (a descendant of l. buccalis). ROSENSTEIN (Berl. klin. Wochenschr., 1867, No. 1) saw the former affection caused by the oïdium albicans.

Concerning the so-called PNEUMONOMYCOSIS SARCINICA, see p. 94.

G. SIMON (Deutsche Klin., 1869, No. 15) found experimentally in man and animals, that small quantities of acid unmixed urine are as harmless as water, that urine mixed with blood, pus and mucus, while urine has an acid reaction, is without injury brought into contact with the surface of wounds or may be injected into the tissues; but that alkaline urine acts destructively upon the tissues, and that all is true of it, which has been traditionally assumed of every urine; that acid urine does not possess the supposed disposition to quicker decomposition, that in intimate contact and mixture with a small quantity of animal tissues and liquids, which had been affected by decomposition, it assumed an alkaline reaction only on the fifth and sixth days, and that in closed vessels it was not yet decomposed on the tenth day; that acid urine in very extensive contact with living tissues and liquids and by long stagnation in the subcutaneous connective tissue does not enter into ammoniacal decomposition; that acid urine, which has been for a long time in contact with dead animal substances, or for a longer time stagnated in the subcutaneous connective tissue of a living animal, assumes no properties which render it destructive of living tissues. Gangrene, which appears so rapidly and extensively in man after infiltration of acid urine, so-called gangrene of urine-infiltration, is, according to S., to be ascribed to pressure from within. If urine in great quantities be forced with great power (by action of muscular coat of bladder and abdominal pressure) into the

stretched intermuscular and subcutaneous connective tissue of the perineum, etc., the nutrient vessels will be lacerated, etc., and thus nutrition will be cut off.

According to MENZEL (*Wien. med. Wschr.*, 1869. Nos. 81–85), gangrene appears after infiltration also of acid urine into bruised tissues.

That putrefying substances, *e.g.*, putrefying tissues from contused wounds, the urine after urine-infiltration, so injurious to fresh wounds, have almost no effect on granulating wounds, is explained by BILLROTH, by the fact that these substances are resorbed only by the lymphatics, but that no open lymphatics are present on the surface of granulations.

The ichor of gangrene, and gangrenous fluids generally often act infectiously on surrounding tissues, unless there early appears a reactive inflammation of them—important in operations in gangrenous parts of every kind.

The poison of dead bodies acts in like manner, likewise the *contagium* in glanders, hospital gangrene, puerperal fever, of the latter of which it cannot be said with certainty, whether it is a specific morbid product or a common product of putrefaction. Here also finally are included many contagious, *e.g.*, that in severe epidemics of scarlet fever, many medicaments, *e.g.*, mercury (gangrenous stomatitis), and many poisons, especially of snakes. It is doubtful whether noma should be regarded as a specific form of gangrene.

The contagiousness of many forms of gangrene, as of hospital gangrene, is doubtful. Many, *e.g.* VIDAL, assume two forms of gangrene of the spleen: a contagious, the carbuncular form, and a non-contagious form, *pustula maligna s. gangrænosa*.

FISCHER (*Char.-Ann.*, 1865, XIII., 1 H., p. 53) concludes from experiments by inoculation, that the secretion of hospital gangrene, as well as the pseudo-membranous and pulpous surfaces of gangrenous ulcers contain an inoculable contagion; that this contagion adheres very strongly to the secretion, and, after standing many days and even after drying, it is still active. The local action began after 24–36 hours. That the resorbed gangrenous ichor acts septically on the blood, is shown by the almost constant icterus of the urine, fatty degeneration of the heart, liver and kidneys. According to BRUGMANS, DELPECH, PITHA and FISCHER, hospital gangrene does not owe its development entirely to a denuded or ulcerating portion of skin, but it may also germinate and increase spontaneously on healthy skin.*

Many causes of gangrene often exist simultaneously. Thus gangrene occurs oftenest in many inflammations, if a light physical or chemical influence on the part is present.

Gangrene occurs for the most part SPORADICALLY. Many forms of it occur EPIDEMICALLY and ENDEMICALLY, *e.g.*, diphtheritis, hospital gangrene, many forms of child-bed fever.

SYMPTOMS OF GANGRENE.

The symptoms of gangrene relate partly to the gangrenous part itself (local symptoms) and its surroundings, partly to the whole organism (general symptoms).

The necrotic part is sometimes sharply defined: GANGRÆNA CIRCUMSCRIPTA; sometimes it is difficult to distinguish the dead from the dying

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* The Editor, in 1863, while serving in the army hospital on David's Island, New York harbor, as medical cadet, U. S. A., inoculated himself twice with products of hospital gangrene without effect. The inoculations were made after the manner of vaccine inoculations, solid gangrenous matter being used on one occasion, and gangrenous ichor on the other: the punctures (on the arm) were covered with a watch-glass and observed. No local or constitutional disturbance followed, although the subject was not in good health.

portions: GANGRÆNA DIFFUSA. Circumscribed gangrene has usually a less, the diffuse a greater extension.

LOCAL SYMPTOMS OF GANGRENE.

They vary with the kind of gangrene, with the blood-supply, and with the character and position of the tissue.

In the gangrenous portions of the body there can be especially distinguished: the gangrenous centre, which, *e.g.*, corresponds exactly with the point of application of the corrosive substance, and the surrounding area, which, surrounding the centre, is of varying circumference (*e.g.*, greatest from sulphuric acid, smallest from the actual cautery), and corresponding to which is the coagulated blood in the arteries and veins. (SAMUEL.)

Formerly, DRY GANGRENE, mummification, whereby the parts become black and dry, was distinguished from MOIST GANGRENE, where they are discolored and soft. At the present time the following forms of gangrene are assumed.

1. So-called DRYING, *i.e.*, that form, where at first only the fluid elements, which lie partly between the tissues, partly within them (cells, fibres), are separated by evaporation or absorption, but besides this almost no morphological changes appear in gangrenous parts. This occurs to the greatest extent in extra-uterine fœtuses (sometimes in twin-pregnancies, where one fœtus dies prematurely, and the other develops further), in intestinal worms in the interior of organs (cysticerci, echinococci, trichinæ), and here affects all tissues. The same process is found to a small extent in the cells of the blood after extravasation into the interior of tissues, of pus and tubercle, more rarely of cancer (so-called simple atrophy, drying, cheesy transformation—see p. 293). In all these cases the parts remain after loss of the water for years unchanged, or the parts afterward calcify. This takes place not by a metamorphosis of the part itself, but it is an infiltration from without; there is formed in grosser parts, *e.g.* in the dead fœtus, first a calcareous shell, while the deeper parts still remain free from lime; smaller parts, as intestinal worms, present calcified cells in their whole thickness.

In the encapsuled fœtus of abdominal pregnancy VIRCHOW and others found after many years muscles, connective tissue, and vessels uninjured.

2. So-called DRY GANGRENE or MUMMIFICATION appears in external parts, when the supply of arterial blood is slowly or quickly cut off, when only the usual amount of blood remains in the parts (without the establishment of a sufficient collateral circulation or a venous and capillary hyperæmia), while besides resorption of fluid tissue-elements, there is also an evaporation of them. This is oftenest the case in gangrene of the bones, also in the extreme portions of the lower extremities in embolic gangrene, and in uncomplicated marasmus, or senile gangrene. The parts, *e.g.*, at first the toes, or the whole foot shrivel into a brownish or blackish, firm mass, sometimes ringing when struck, but retaining its form. A similar thing occurs in the various forms of gangrene from pressure, when in consequence of pressure they have at the same time become to a high degree anæmic: the gangrenous parts then have mostly a white color.

3. So-called SOFT GANGRENE,—or, since no badly smelling gases are generated, ODORLESS GANGRENE consists in a simple SOFTENING, *colliquatio*, without putrefaction. In this form the tissues become liquid: the fluids

arise within the tissues themselves or enter them from without. Soft gangrene occurs in normal tissues, most frequently as WHITE SOFTENING OF THE BRAIN after embolism of the cerebral arteries with no collateral circulation. It occurs also in thrombi, sometimes in hæmorrhagic accumulations in organs, to which air cannot have access, in chronic pneumonia, perhaps also in abscesses. It has been longest known as SECONDARY SOFTENING or LIQUEFACTION of tubercles (in the brain, lymph-glands, etc.) and cancers, where it begins in the centre of the new formation, and in its progress on the periphery in flat organs gives rise to ulcers.

Just such a case was seen by myself, where a woman 46 years old, after having been affected by peliosis for two years, and by diarrhœa for nine months, died. The autopsy revealed in the lower portion of the jejunum and the entire ileum about sixty round, elongated, dentated, etc., gangrenous spots of a yellowish-white color and of the size of a lentil to that of a dollar, which affected only the mucous membrane or all the coats of the intestine, which they nearly or wholly perforated and which were the causes of the fatal purulent peritonitis. The genesis of this gangrene has heretofore remained unknown.

4. True PUTREFACTION, PUTRESCENCE, SEPSIS most commonly appears in the same manner, as every animal substance putrefies through access of air and the presence of abundant water: so-called MOIST GANGRENE, GANGRENE, SPHACELUS. All soft parts of the body putrefy, as soon as the vital transformation of material in them ceases; for the most part quickly in proportion to the amount of blood in the tissues (from previous hyperæmia), their softness, and water contained in them (fatty tissue, connective tissue, muscles). The ferment is partly contained within themselves, and is partly received from without. Moist gangrene occurs in external parts of every kind, especially also in disintegrating soft new-formations of them: it is the common form of pulmonary gangrene. (See p. 101.)

Sometimes decomposition progresses to the development of gases: EMPHYSEMATOUS GANGRENE.

In gross the external parts in moist gangrene appear at first looser, more flaccid, doughy, discolored; sometimes the coloring matter of the blood settles and there appears a dark, bluish, or dark red coloring. The epidermis, or the whole epithelial layer is raised in blisters, which are filled with a reddish or brownish fluid (so-called gangrene-vesicles); beneath them especially, putrefaction goes on. The parts break up with great stench at first into ragged, withered, then greasy and liquid masses of blackish, brownish, yellow appearance. Some portions dry up, others fall off or remain attached to tendons, ligaments, bones. In gangrene of whole extremities, destruction of the skin and connective tissue for the most part progresses further than that of the muscles, and the latter further than that of the bones. The sulphuretted hydrogen generated colors silver probes and lead ligatures black through the formation of the sulphide of silver and sulphide of lead. Pulmonary gangrene behaves in a similar manner, in which besides the flaccidity, anæmia, etc., of the tissue, the stench is especially characteristic.

Under the microscope the tissues in moist gangrene appear at first only clouded, retain their form, but later break up always into smaller colorless particles—so-called gangrenous detritus. At first the blood-corpuscles and fat-cells are destroyed: the parts are impregnated with the coloring matter of the blood; fat is found mostly in very great quantity, mostly free, partly in crystals. The former depends for the most part upon the destruction of tissues, in part perhaps also upon an infiltration from without.

The so-called gangrenous ichor consists chiefly of water, decomposed blood and fat, and molecular masses. Gland-cells and epithelium are destroyed almost as quickly; then follow muscles and nerves. Connective tissue and cartilage last longer, the horny tissues, elastic tissue (*e.g.*, in arteries, bronchi, lungs), hyaloid membranes, bones and teeth last the longest. As microscopical objects, finally, there are seen chiefly granular masses (albuminous molecules, fat-granules, pigment-granules), larger pigment-masses, fat-drops, fat-crystals, cholesterin, crystals of chloride of sodium, triple phosphates, of sulphate and carbonate of lime, sal-ammoniac, leucin. Besides, there occur, according to the form of gangrene, various fungi (bacteria, mould-fungi, etc.). The chemical elements are butyric acid, valerianic acid, carburetted hydrogen, ammonia, sulphuretted and phosphoretted hydrogen, sometimes nitrogen: by which is explained the color and odor of gangrenous masses.

The histological changes of gangrenous parts are not characteristic. DEMME'S so-called gangrene-corpuscles occur also under other conditions. The changes and final destruction of red blood-corpuscles have been investigated, especially in cases of experimental burning (M. SCHULTZE, WERTHEIM, FALK).

The so-called gangrenous fœtuses are very different. They are of various ages. All tissues show essentially a soaking with sero-bloody liquid; the serous sacks contain the same. The softer tissues are in part dissolved; almost all are dirty-red from diffusion of the coloring matter of the blood. The odor of such fœtuses is, on the contrary, stale; stinl ing, only when after the escape of the fœtal liquid air takes its place.

Concerning the microscopical conditions, see BUHL (HECKER and BUHL, *Klin. d. Geburtsk.*, 1861, p. 326). In a peculiar "lipoid transformation" of a fœtus B. saw the walls of the cavities of the body covered with a thick layer of grayish white grease (needles of margarin).

A MOULDING of the gangrenous part may be combined with each of the four kinds of gangrene. (See p. 95.)

The four kinds of gangrene mentioned, as well as the circumscribed and diffuse gangrene, may pass in many ways into one another. Thus we see, *e.g.*, in *gangræna senilis*, on the surface dry gangrene, under the skin moist gangrene: moist gangrene becomes dry or mummified, if it occupies external surfaces and the affected portion of skin is not too thick, so that it can dry out. In embolic gangrene, common mummification is often found in the toes, while in the upper portion of the thigh moist gangrene is commonly present.

In HOSPITAL GANGRENE (*gangræna nosocomialis*) fresh as well as granulating and cicatrizing wounds are affected in a peculiar manner. Either the granular surface is changed into a yellowish greasy pulp, which can be wiped off the surface, but whose deeper layers are firm. The surrounding skin shows the same metamorphosis, so that the original wound is after 3–4 days increased to double its size. Or a wound quickly assumes a crater-like character, and secretes a sero-ichorous liquid, after the separation of which the tissues lie free. This takes place usually in tolerably sharp circular forms and not infrequently to a considerable depth. These changes occur especially in trifling wounds, like leech-bites, wounds from cupping instruments, even vesications of blisters. Both forms are known as pulpous and as ulcerous hospital gangrene.

The VOLUME of gangrenous parts and organs is, according to the form of gangrene, normal, increased or diminished.

The COLOR of gangrenous parts is sometimes unchanged, sometimes white (so-called white gangrene from local anæmia or infiltration of pus), sometimes one of the most various shades of gray, grayish-blue, grayish-green, brownish-red, brown, black. The latter colors are dependent upon infiltration of the coloring matter of the blood, or at the same time upon the formation of sulphide of iron.

The ODOR of gangrenous parts sometimes cannot be perceived, sometimes it is (in putrefactive gangrene after destruction of the skin, in pulmonary gangrene, etc.) peculiarly sweetish, or is in the highest degree stinking.

PALPATION shows the temperature of gangrenous parts lowered since it is only communicated from the surrounding structures. According to the form of gangrene is the consistence hard, or flabby, or there is to be felt a peculiar crepitation (emphysematous gangrene).

The FUNCTION of gangrenous parts is completely destroyed. Sensation and motion are wanting in external parts. That the former is sometimes still present is explained by the known law, that irritation of a nerve-fibre in any part of its course is always felt at its peripheric extremity. That motion is sometimes present in gangrenous extremities, comes from the fact, that in gangrenous parts tendons are found, whose muscles are above the gangrenous centre. By the action of gangrenous substances on the surrounding structures there arise various forms of functional disturbances : in the lungs, often tormenting cough.

PAIN is mostly wanting in gangrene even of external parts rich in nerves, e.g., in most cases of gangrene from pressure; it is more rarely present, as in many cases of *gangræna senilis*, when preceded by inflammatory phenomena, in all cases of embolic gangrene after endocarditis (so-called rheumatic gangrene). If it is the extremities which are gangrenous, they feel to the sick person like a dead burden. If the part has experienced severe pain before the appearance of the gangrene, there follows with its appearance a relief from suffering; on the other hand, pains of the upper part are readily referred to the insensible periphery. Smaller gangrenous centres in the interior of the lungs, brain, etc., especially in parts with small supply of sensory nerves, are wholly painless.

The vicinity of gangrenous parts is often hyperæmic and œdematous.

The local symptoms of gangrene sometimes appear quickly, sometimes slowly—variations which depend chiefly upon the kind and intensity of the cause, as well as the kind of tissue.

The beginning of the local symptoms of gangrene varies sometimes in the same form of gangrene. Gangrene from decubitus, *e.g.*, begins sometimes as a local, very painful inflammation, which passes into ulceration and then into gangrene ; or there appear at first bluish-red spots, which become blisters or are immediately transformed into gangrenous sloughs.

In a case, reported by ROSENTHAL (*Wien. med. Jahrb.*, 1872, p. 389), where there was an ischæmic paralysis of the extensor muscles of the thigh of the left side from an aneurism of the femoral, loss of electro-muscular contractility on the extensor side of the thigh preceded by one day the appearance of the first signs of gangrenous destruction of the soft parts.

THE GENERAL SYMPTOMS OF GANGRENE are often wanting, if the gangrene affects only small portions of internal or external parts, if it consists in a simple atrophy and drying, if its cause is a purely external one, and if the gangrenous portion is encapsuled, or the connection with normal surrounding tissues is destroyed. On the other hand, they are present, especially if the gangrene is greatly extended, if it has extensive contact with sound tissues, if the latter are not protected by early thromboses, or granulations.

They follow most quickly in extended destructive gangrene and in moist gangrene chiefly, especially in many cases of pulmonary gangrene.

They give rise to the so-called GANGRENE-FEVER (septicæmia, ichorrhæmia). It is characterized by great collapse (paleness, loss of strength, etc.), for the most part elevated temperature, small and frequent pulse, accelerated respiration, great thirst, etc., repeated shiverings or chills (so-called *intermittens perniciosa*). At other times, phenomena similar to those of cholera are present, especially severe diarrhœa. Or there are profuse sweats. These, as well as vomiting, sometimes exert a favorable influence. In hospital gangrene gastric symptoms are often prominent. The fever is for the most part inversely to the limiting inflammation, and proportionate to the moistness of the gangrene. It is usually irregularly remittent.

After burning of the skin there appears at first a quick, then a slow lowering of the temperature, which continues until death : this has been demonstrated by numerous experiments, as well as by observations on man (BILLROTH saw in one case a temperature of 33 C.). The cause of this lies, according to FALK (*Virch. Arch.*, 1871. LIII., p. 27), in the increased loss of heat through the very hyperæmic skin : heat diminishes or destroys the elasticity of the vessel-walls, so that the vessels are dilated by the blood-pressure ; since the afferent branches are not dilated, the increased size of the current must cause a slowing of it. Diminished temperature of the blood depresses further the action of the heart, which, thereby as well as by the enlargement of the vessels, may be paralyzed. The cooled blood may also paralyze the nervous system (drowsiness—more infrequent respirations). Inflammations of the lungs and kidneys, as well as duodenal ulcers not infrequently occurring in those who have been burned, are explained by F. by the depressed heart's action, the character of the blood, the latter besides by the corrosive action of the intestinal contents.

General infection is dependent upon the appearance of gangrenous masses in corroded, non-thrombosed veins, with consecutive embolism, but especially upon the resorption of putrid liquids by means of the blood- and lymph-capillaries.

An embolism of fungi also has been shown in consequence of primary gangrenous processes. WALDEYER (*Virch. Arch.*, LII., p. 541) saw in *gangræna senilis* of the hand pigmented bacterian colonies in both kidneys. I saw non-pigmented bacteria, beautifully colored blue by hæmatoxylin, in the bloodvessels of hæmorrhagically inflamed kidneys in senile gangrene of the foot.

KUSSMAUL (l. c.) has shown that a putrified member is not to be regarded merely as a dead appendage, even if there is no longer a blood-circulation ; that rather there may exist an active interchange of juices with living parts; that the mechanism and even the chemical action in sphacelus differ from those in the putrefaction of dead bodies ; that, finally, the danger in gangrene of a member depends not only upon the extent of contact of living with dead parts, but also on the size of the whole putrid mass. When, for example, all the blood-currents in the leg and greatest part of the thigh had been arrested in consequence of thromboses, and iodide of potassium, in concentrated solution, injected under the sole of the foot, already after four and a half hours it appeared in the urine, and its excretion continued in increasing quantity for twenty-four hours until the death of the animal.

A. KEY and WALLIS (see p. 251) showed that numerous white blood-corpuscles immigrated into the slough, produced by corrosive action, of the cornea of the frog.

COURSE AND TERMINATION OF GANGRENE.

Diffuse gangrene progresses either to the death of the individual ; or it becomes limited and circumscribed.

In a favorable termination, thrombosis calls forth in the gangrenous part a collateral hyperæmia of the surrounding textures, the gangrenous portion itself acts as an irritant on the surrounding tissues and causes inflammation

of them. There appears the so-called LINE OF DEMARCATION, i.e., a lighter line of tissues, which has become hyperæmic and is suppurating. It fol lows for the most part the contours of the gangrenous mass. It is at first mostly superficial, but gradually deepens and finally separates the slough or gangrenous mass from the healthy structures. By the violent removal of the slough, light hæmorrhages occur, which in a slow and spontaneous separation is prevented by thrombosis. The dangers of demarcation vary with the surrounding tissues: e.g., typhous ulcer of the intestines, skin, lungs (in the latter almost always ichorous pleuritis and pneumothorax). The time which intervenes until the dead is wholly separated from the living structures varies greatly with the structure and the vascularity of the tissues. Demarcation takes place most quickly in very vascular soft ulcers, in subcutaneous cellular tissue and in the muscles, more slowly in the corium and mucous membranes, slowest in veins, fasciæ, and, of all others, in bones. The time depends also upon the volume of the gangrenous part and the general condition of the individual. The loosening or throwing off of gangrenous parts most commonly occurs in necrosis of surfaces which are in contact with the air (skin, mucous membranes, lungs), if life has not previously been destroyed.

Sometimes, especially with dried portions in internal parts, a connective tissue is formed through limiting inflammation, and, by means of connective tissue or osseous new-formation, there results an encapsuling of the necrotic part, e.g., tubercles, typhoid sloughs, portions of bone.

SAMUEL has experimentally investigated the influence of arterial ligature on the origin and course of gangrene. Direct use of caustics cause in anæmic parts as quick and extensive cauterization as in normal parts, but the limiting inflammation is delayed. The same caustics, on the other hand, which at first excited inflammatory swelling, and only then gangrene (chloride of zinc with muriatic acid, etc.), act considerably more slowly. Etc.

A healing of gangrene is possible only in the sense that the gangrenous part is encapsuled, or thrown off. The former takes place only under certain conditions. A throwing off occurs much more frequently, and is more or less easily accomplished, according to the size of the gangrenous part, or according to its superficial or deep extent, but in internal parts it occurs for the most part very slowly. A cicatrix usually remains behind in place of the gangrene.

Special examples of these various possibilities of recovery are afforded, by the separation of gangrenous members, in which art must often be used to assist; by separations of superficial diphtheritic portions of mucous membranes, and that of typhoid sloughs on the mucous membrane of the intestine. Still more difficult is the removal of gangrenous portions which are located within bones or parenchymata, as that of central bone-masses and gangrenous portions of lungs; canals leading from gangrenous cavities to the surface are called CLOACÆ. In furuncle and carbuncle there first appears necrosis of a portion of cutis or subcutaneous fat-tissue, and around this the abscess forms.

A necrotic part cannot be resuscitated. An apparent death may exist in embolism; the anæmic part may appear pale, cold, and paralyzed; but even then it is not gangrenous, but becomes so only when the blood-supply remains cut off for a long time; only when a collateral circulation is established does life often return. A second apparent exception of healing after the appearance of gangrene is met with in incarcerated portions of intestines.

See SCHWENINGER, Arch. d. Heilk., 1873, XIV., p. 300.

Gangrene acts BENEFICIALLY only in comparatively rare cases, where products of inflammation (pus) are destroyed by it, or where new-formations (typhoid sloughs, hæmorrhoidal tumors, or like formations, polypi) are thereby removed.

Gangrene terminates UNFAVORABLY, in part because of local disturbances, in part also because of the general infection of the body.

Dangerous local disturbances are dependent partly upon the gangrene itself, partly upon the inflammation, which limits it. They are: perforations (as of gangrenous lungs into the pleura; typhous intestinal ulcers and gastric ulcers into the peritoneum); dangerous hæmorrhages in consequence of incomplete or wholly absent thrombosis, great blood-congestion, diseases of vessels, etc. (of extremities, stomach, intestines); inflammations of serous membranes with ichorous exudations on important organs, e.g., on the brain. Or the body is exhausted sometimes by mere inanition, sometimes in the form of hectic fever, in which there is great painfulness, with wearing away of parts.

Dangerous general disturbances, which arise in consequence of gangrene, are in their higher degrees usually fatal.

Autopsies under such conditions furnish nothing characteristic besides the gangrene, the reactive inflammation, and the causative changes. Common or so-called croupous inflammations of the intestines are sometimes met with. Metastatic foci occurring in many organs have sometimes a gangrenous character (so-called METASTATIC GANGRENE).

3. PROGRESSIVE METAMORPHOSES.

(REGENERATION, HYPERTROPHY, TUMORS.)

ABERNETHY, *Surgical Works*, 1811, II.—HOME, *On the Formation of Tumors*, 1830.—J. MÜLLER, in his *Archiv*, 1836.—Idem, *Ueber den feineren Bau und die Formen der krankhaften Geschwülste*, 1838.—HAWKINS, in *London Medical Gazette*, 1837-8.—WARREN, *Pr. Bemerk. über Diagn. u. Cur. d. Geschw.*, 1839.—VOGEL, *Gewebe in pathologischer Hinsicht*, in Wagner's *Handwörterbuch der Physiologie*, 1842, I., p. 797.—BREUER, *Melet. circa evolut. ac formas cicatricum*, 1843.—BÜHLMANN, *Beitr. zur Kenntniss der kranken Schleimhaut, u. s. w.*, 1843.—REINHARDT, *Traube's Beiträge*, 1843, II.—Idem in *Virchow's Archiv*. I., p. 528.—J. and H. GOODSIR, *Anatomical and Pathological Observations*, 1845.—BRUCH, *Die Diagnose der bösartigen Geschwülste*, 1847.—VIRCHOW, *Würtzburg. Verhandl.*, 1850, I., pp. 81 and 134; II., p. 150.—Idem, in his *Archiv f. path. Anat.*, I., p. 94; IV., p. 515; VIII., p. 371; XI., p. 89; XIV., p. 1.—Idem, *Die krankhafte Geschwülste*, 1863, I.; 1864-5, II.; 1867, III., Th. 1.—FÜHRER, *Deutsche Klinik*, 1852.—PAGET, *Lectures on Tumors*, 1851.—SCHRANT, *Prijsv. over de goed-en kwaadart. gezw.*, 3 Aufl., 1852.—REMAK, *Müller's Archiv*, 1852, p. 47.—ROBIN, *Gazette Médicale*, 1853, No. 51.—CHUR, *Ueber d. Erk. d. Pseudoplasm.*, 1854.—HIS, *Beitr. z. norm. u. pathol. Histologie der Cornea*, 1856.—WITTICH, *Virchow's Archiv*, 1856, IX., p. 185.—O. WEBER, *Virchow's Archiv*, 1858, XII., p. 74; XXIV., pp. 84 and 163.—Idem, *Handb. der Chirurgie*, 1865, I., p. 240.—BILLROTH, *Beiträge z. pathol. Histologie*, 1858.—Idem, *Deutsche Klinik*, 1859, No. 40 et seq.—RINDFLEISCH, *Virchow's Archiv*, 1859, XVII., p. 239.—Idem, *Experimentalstudien uber d. Histologie des Blutes*, 1863.—VON RECKLINGHAUSEN, *Virchow's Archiv*, 1863, XXVIII., p. 157.—THIERSCH, *Der Epithelialkrebs nam. der Haut*, 1865.

[PAGET, *Lectures on Surg. Path.*—BILLROTH, *General Surg. Pathology.*—RINDFLEISCH, *Pathological Histology.*—ED.]

On regeneration, consult: SPALLANZANI, *Opusc. di fisica. anim. e veget.*, 1776.—ARNEMANN, *Verh. über d. Regeneration, an lebend. Thieren.*, 1783.—MURRAY, *De redintegrat. part. corp. anim. nexu suo sol. vel amisso*, 1787.—BLUMENBACH, *Ueber d. Bildungstriebe*, 1791.—EGGERS, *Von d. Wiedererzeugung*, 1821.—DIEFFENBACH, *Nonn. de regen. et transplant.*, 1822.—H. MÜLLER, *Verh. d. Senck. Gesell.*, 1864, V.,

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p. 113.—Works on plastic surgery, on the reproduction and new-formation of connective tissue, bone, muscle, nerves, bloodvessels, etc.

On the reunion of parts almost or wholly separated from the body, consult more especially: HALLER, *Element. physiol.*, 1766, t. VIII. sect. II., p. 162.—WIESMANN, *De coalitu partium a reliquo corpore prorsus disjunctarum*, 1824.—DIEFFENBACH, *Graefe-Walther Journal*, 1824, VI., p. 122.—ZEIS, *Literat. u. Geschichte d. plast. Chirurgie*, 1863, Nos. 213–422, etc.—HANFF, *Ueber Wiederanheilung vollständig vom Körper getrennter Hautstücke*, 1870. (See also New-formation of Bone.)

Compare besides, the older works of GALEN, INGRASSIA, FALLOPIUS, ASTRUC, PLENCK, and others; as well as the newer treatises on pathological anatomy and surgery, and monographs on special points.

PROGRESSIVE METAMORPHOSIS consists in the production of one or more new tissues, similar to, or varying in various ways from normal tissues.

Pathological new-formations are either: HYPERTROPHY IN GENERAL, HOMŒOPLASIA, HOMOLOGOUS NEW-FORMATIONS, that is to say, tissues which resemble normal parts of the organism in size, shape, arrangement, function, etc.; or: the so-called HETEROPLASIA, HETEROLOGOUS NEW-FORMATIONS, that is to say, tissues which bear but little resemblance to normal tissues.

New-formations are divisible into three classes, which present several intermediate transition forms; as:

REGENERATION, that is to say, the new-formation of a part which has been destroyed;

Or as HYPERTROPHY, that is to say, the new-formation of tissues of same appearance and function as the part affected:

Or as TUMORS, that is to say, a new-formation in striking contrast to its surroundings, of a structure not at all, or seemingly not at all different in its histological elements from the parts affected, but unlike it by its numbers, size, shape, arrangement, and function.

REGENERATION, the renewal of a destroyed tissue, is a process which ranks half way between normal and pathological new-formations. It is very probable that gradually all the tissues of our body are reproduced: at any rate this is certainly true of the hair, nails, the stratified epithelia, of striated and smooth muscular fibres; it is almost certain of all true epithelia, of gland-cells. The term pathological regeneration is employed consequently when we speak of a renewal of tissues whose destruction has not been brought about by the normal exercise of their functions, but by the action of certain influences whose derivation is outside the limits of health.

The regeneration may be a true or complete one, that is to say, there arises a tissue just like the one destroyed (epidermis, epithelium, hair, nails, connective tissue, bony tissue, nerves, occasionally muscular substance, the crystalline lens, or possibly the vitreous body). Or, the regeneration is imperfect, that is to say, cicatricial tissue is formed where loss of substance has occurred (external skin and mucous membranes, glands, etc., not rarely also in muscles). This cicatricial tissue either does not undergo further change, forming permanent scars, or its place is after awhile occupied by normal structures, provisional scars.

In the external parts (skin and bones) regeneration can be directly observed: in other parts we are obliged to infer its occurrence from the restoration of function—as in nerves; and under other conditions it can only be determined by minute, exact, or even microscopic examination.

In the human species regeneration is obtained only in the case of simple tissues (epithelia, connective tissue), or in the case of tissue-systems (bloodvessels, bones, muscles), never whole organs or parts of organs. In the lower animals regeneration takes place on a very much greater scale; in salamanders and lizards reproduction of

the tail and even of its contained spinal cord has been seen; in tritons whole limbs, the lower jaw, even the eye, have been regenerated.

THE REUNION OF WHOLLY DETACHED PARTS is closely allied to regencration. This reunion usually only takes place if the separated parts have been severed from the body only a short time, so that it be yet warm and viable. As examples may be cited the reunion of teeth (even dead teeth have been known to revive in an alveolus), hairs, bones, wholly separated bits of skin from various parts of the body, separated noses, ears, whole phalangeal portions of fingers. These parts are not merely in vascular, but also in nervous union with the original body; even lupus and epithelial cancer invade such parts, sometimes with especial readiness.

The compensatory development of organs remaining in the body, and having a structure and function similar to those of the lost part, belongs in part here, but in part also enters into the domain of hypertrophy. For example, the development of small arteries and veins into larger vessels in the collateral circulation; the hypertrophy of one kidney after atrophy of the other; the hypertrophy of the lymphatic glands after extirpation of the spleen, etc.

HYPERTROPHY is either a simple, true hypertrophy, in which the tissue-constituents exist in normal number, but are enlarged; or is a numerical hypertrophy or hyperplasia, in which the important tissue-elements, or all of them, have increased in number. The simple and the numerical hypertrophies often pass into one another, and are even exhibited within physiological limits, as in muscles and bones. Hypertrophy sometimes affects whole organs (muscles, bones, adipose tissue); sometimes only parts of organs, when it is immaterial whether we call the growth hypertrophy or tumor (as, for example, hypertrophy of the papillary layer of the skin, wart, or condyloma; local hypertrophy of the mucous membrane, or mucous polypus; partial hypertrophy of bone, osteophyte or exostosis). The localized or generalized hypertrophies of the connective tissue, in the midst of which the more important elements, muscular fibres, glandular cells, are preserved or reduced in number, are commonly called indurations or scleroses.

TUMOR-LIKE NEW-FORMATIONS, OR TUMORS (growths, neoplasmata, pseudo-plasmata, are, histologically speaking, homœoplastic or heteroplastic (*vide supra*); their relation to surrounding parts is such that they are either circumscribed or diffused. Circumscribed growths are usually globular or knotty masses which have pushed normal tissues to one side; in diffused or infiltrating growths, on the contrary, the elements of the tumor are so deposited between the elements of the normal tissue that there is no separation between them; or else the elements of the tumor occupy the place of the normal elements which have been destroyed (so-called substitution).

It is not possible to give an exact definition of the word TUMOR, either in the above meaning of the word, or in a more general application. In the latter sense we speak of tumor of the spleen, tumor of the face, without meaning tumor in the former sense. Küss would designate an inflammatory tumor as phlogoma. Tumors may, as wholes, deviate a great deal from a normal tissue, but their ultimate elements, cells, fibres, etc., are formed like the cells and fibres of normal tissues, and joined together according to the same laws. Tumors do not differ from normal tissues by the presence of specific elements; but often they are not even abnormally constructed, but are abnormal (pathological) only because they occur in a locality in which their elements do not normally exist (Heterotopia); or because they are developed at a time when their presence is an abnormality (Heterochronia). Consequently, VIRCHOW calls tumors which are composed of only one tissue (for example, epithelium, or connective tissue), tissue-like, or HISTIOID; those composed of several tissues, organ-like, or ORGANOID; lastly, those composed of several tissues and organ-like parts (as tumors of the skin com-

posed of connective tissue, epidermis, sweat and sebaceous glands, etc.), SYSTEMA-TOID, or TERATOID. In addition, there are tumors in which several types of tumors are combined, combination tumors, *masses dissimilaires, productions mixtes.*

The occurrence of hypertrophies and new-formations in various organs and tissues varies. Some occur in all or almost all tissues or organs, as especially the connective tissue and vessels, tubercle and cancer; this takes place either with almost equal or with varying frequency (see the scale of frequency of tubercle and cancer). Many new-formations occur only in certain organs and tissues, in which case the latter and the new-formed tissue mostly agree in structure: connective tissue occurs oftenest in connective tissue; osseous tissue, oftenest in bones and periosteum; fat-tissue, almost only in fat-bearing parts, organic muscle-fibres, almost only in organs made up of this tissue, epithelial and glandular tissue, almost only in like epithelial and glandular organs, etc. The tissue, from which all new-formations, with the exception of the epithelial, most frequently proceed, the so-called general germ-tissue of the body, is connective tissue in all its forms.

The NUMBER of new-formations in an individual varies greatly. Either only one or several are found, or their number is very great, innumerable. In the latter case new-formations either vary in structure, their occurrence together is accidental (*e.g.*, enchondroma and cancer); or they have a similar structure (*e.g.*, cancers). If new-formations exist in great number, they are located in the same organ or tissue (*e.g.*, myoma in the uterus, enchondroma in the bones); or they are located in different organs (*e.g.*, cancer in the stomach, liver, and lungs).

The SIZE of new-formations varies from an extremely small size, not at all or just perceptible (*e.g.*, so-called miliary tubercle and cancer), to that of a cherry, egg, the fist, and larger. Many become colossal in volume, and weigh as much as 50 kilo.

The FORM of new-formations is likewise variable, and depends partly upon the place of development, partly upon unknown conditions. Diffuse hypertrophies have in general the form of the mother-organ. Tumors are oftenest round, roundish, more rarely irregular; otherwise flat, smooth, or globular. They are connected by their whole circumference with the mother-organ, or only at one point (so-called peduncular, polypoid tumors): these have their origin especially in proportionately narrow spaces, with indentations. The surface of new-formations is smooth, or uneven, or lobed. New-formations occurring on the surface of the skin, mucous, serous, and synovial membranes, have been for the most part named: circumscribed or partial hypertrophies, or flat or insular swellings in their lower grades, polypous swellings, polypus, fungus in their higher grades; in many special cases also dendritic growth.

The CONSISTENCE of new-formations depends essentially upon structure and metamorphosis, and presents every imaginable degree.

The elements of hypertrophies and new-formations are, on the whole, the same as those of normal tissues. They are granules, nuclei, cells, basis substance of the most different kinds, especially connective tissue and osseous tissue, also vessels, etc.

Pathological cells, on the whole, are like physiological cells, in their histological and chemical properties (size, substance, form of body of cell, cell-membrane, nucleus, etc.), as well as in their vital phenomena (growth, accretion, excretion, increase, the ability of some to change their form and place: fixed or immovable cells as connective-tissue cells, epithelial cells,

gland-cells, etc., or wandering, amœboid cells, so-called leucocytes, as color-less blood-corpuscles, wandering cells of connective tissue); these peculiar-ities occur collectively within the widest limits. Besides the cells proper, there are often found at the same time, so-called PROTOBLASTS (primitive germs, cytoblasts, cell-germs, germ-cells), *i.e.*, bodies which consist of a nucleus surrounded by a viscous or mucous, bright or granular substance (protoplasm), which is sometimes thickened peripherically, but membrane-less: these are identical with white blood-corpuscles, lymph-corpuscles, wandering cells, cells of medulla, lymphoid corpuscles. Bodies also are not infrequently found, which consist of a nucleus and of a cortical sub-stance surrounding it only at points. Finally, there are true FREE NUCLEI. The nucleus is the most important element as well of cells proper, as of protoblasts: it regulates the function of the cell (the appropriation and excretion of nutritive material, the metamorphosis of cell-contents, etc.), and is most essentially concerned with the increase of cells.

There is constantly found between the cells a more or less abundant, fluid or solid INTERCELLULAR SUBSTANCE, which in the first case is probably analogous to the so-called tissue-cement, and is mostly colored black by nitrate of silver.

On the unessential nature of the cell-membrane consult especially SCHULTZE (*Müll. Arch.*, 1861, p. 1) and BRÜCKE (*Sitzungsber. d. Wien. Acad.*, XLIV., p. 381: "*Ele-mentarorganismen*"). BEALE divides the elementary parts of a tissue into a living or germ-substance (germinal matter, SCHULTZE'S *protoplasm*), and a lifeless or formed substance (formed matter). The former is colored red by an ammoniacal solution of carmine; the latter remains uncolored. The former grows, is active and is the seat of changes; the latter proceeds from the germ-substance, but is passive and cannot grow; it is external to the former and becomes thicker from deposits of new material on its internal surface. According to SCHWEIGGER-SEIDEL (*Arb. aus. d. phys. Anst. zu Leipzig.*, 1870, IV., p. 121), all cells and their descendants consist of two substances: the one is the seat of physiological function, and in different cells possesses varying physical and chemical properties; the other is common to all cell-forms and is truly formative, as stroma; or appear rather as a deposition be-tween the more sharply defined morphological groupings of the first substance (*e.g.*, in transversely striated muscles). Upon it depends the occurrence of myosin.

Pathological cells are in part more easily changeable and destructible than phy-siological cells. Various changes worthy of note appear, especially after the addition of water. (See p. 335.) Many cells are then found uniformly or irregularly enlarged, clearer or more clouded, sometimes entirely destroyed. Or, the water entering the cell aggregates into a sharply defined, round light spot of varying size and presses the remaining granular cell-contents, sometimes also the nucleus to one side. Or, many such spots appear in the cell-contents, through the projection for-ward from the cell-membrane of round hyaline globules, which separate, swim away and disappear.

The distinction, above given, between fixed and movable cells has recently been rendered untenable, since phenomena of motion have also been observed in epithe-lial, glandular, cancer cells, as well as in connective-tissue corpuscles. HELLER (l. c.) has observed on the warmed object-plate movements of the epithelium of a frog's tongue on the borders of spots where tissue has been lost, WALDEYER (*Virch. Arch.*, 1872, LV., p. 67) has observed the same in epithelial cells of two mammary cancers.

The PATHOLOGICAL PRESENCE OF CELLS presupposes either a wandering of them into the locality, or a new-formation in the locality itself.

The migration of cells, which until now has been demonstrated only with respect to colorless blood-corpuscles, or pus-corpuscles, belongs, according to many, also to some others, cells hitherto regarded as elements of pure new-formations, as those of cicatricial tissue, tissue of pseudo-mem-branes, of hyperplastic connective tissue especially, perhaps also those of new-formed muscles and nerves.

Since the discovery of the migration of colorless blood-corpuscles (see p. 152), those new-formations, which at first consist of small, round cells not to be distinguished from the blood-corpuscles named, are no longer to be regarded as products of epithelial cells, or of false epithelium, or of connective-tissue corpuscles, but in all doubtful cases it must be inquired into, whether these also are migrated blood-corpuscles.   In the human living and dead body we have heretofore employed for this distinction only negative means; the demonstration of younger stages of development of cells from epithelium or from connective-tissue cells, etc., is opposed to their migration.   So-called feeding of white blood-corpuscles with coloring matters has been employed in investigations on animals with respect to this distinction. (See p. 154.)   Many regard the round, indifferent cells, containing the coloring matter, as emigrated blood-corpuscles and not as new-formed cells: RINDFLEISCH, O. WEBER, KREMIANSKY, MASLOWSKY, AUFRECHT, and others.   In this, no one goes so far as BILLROTH (*Oestr. med. Jhrbb.*, 1869, XVIII., 4 et 5 H., p. 3).   Molecules of coloring matter probably however enter into young cells of every kind, *e.g.*, epithelium.   And since such molecules, after injection into the blood, are found not only in colorless blood-corpuscles, but also free in epithelium, cartilaginous tissue, etc. (see p. 155), conclusions drawn from such experiments are to be received with caution.

NEW-FORMATION OF PATHOLOGICAL CELLS takes place from pre-existing normal or pathological cells: either by division, or by endogenous cell-formation.   The origin of the cell always precedes that of the nucleus. In almost all cases there is a simultaneous increase of the protoplasm.

CELL-DIVISION affects the cell in toto, *i.e.*, all the parts of it (membrane, contents, nucleus and nucleolus).   It takes place for the most part in the long, rarely in the transverse axis of the cell.   By division there are at first usually only two cells formed, rarely three or more, at the same time: they are for the most part smaller than the original cell.   The division itself affects first the nucleolus, then the nucleus, which become elongated, and then constricted in the middle and divided; the protoplasm at the same time increases in quantity.   After complete division of the nucleus, the cell at first shows a depression at one point, which then continues around the cell and finally divides it, so that two (or even three or more) cells are formed with nucleus.   Division of cells, and especially that of the nucleus, is accomplished quickly, within a few seconds, so far as observations have demonstrated this in living cells and on the warmed object-plate.   It not infrequently retrogrades, after it has already progressed very far.   It is rarely observed in epithelial cells.

KLEIN (*Med. Ctrlbl.*, 1870, No. 2) observed division of the colorless blood-corpuscles of the triton, as well as of the frog, from cleaving of a previously formed connecting filament, as well as by constriction.   In man he observed only the latter.   The corpuscles of triton's blood may divide more than once. HOFFMANN agrees with these views.
STRICKER describes a third form of division in wandering cells of the tongue and cornea of the frog (*Studien.*, 1869, I., Cap. II.).

BUDDING, so-called, is a variety of cell-increase by division.   After single or manifold division of the nucleus, one or many nuclei advance to the periphery of the cell.   The latter protrudes at these points like buds, and at the same time a nucleus enters each bud.   Finally the bud separates and becomes a free nuclear cell.

Consult also LANG (*Virch. Arch.*, 1872, LIV., p. 85).

ENDOGENOUS CELL-FORMATION (endogenous cell-division) consists in this: the nucleus, after previous division of the nucleolus, divides into two,

rarely into many, nuclei. With the simultaneous enlargement of the cell
the new-formed nuclei divide, etc., so that, finally, a cell is formed with
4, 8 and more nuclei.

The cells, in a series of cases, remain unchanged : so-called mother-cells
with daughter-cells—GIANT-CELLS, MYELOPLAXES. This process is found
especially often in cells without a proper cell-membrane. Then there arise
for the most part finely granular masses of varying size, even macroscopi-
cal, round or rounded or provided with numerous processes, according to
the density of the surrounding tissue, and containing, the majority of
them, 10, 20, 50 and more peripherically placed nuclei. They occur
physiologically in bone-marrow, pathologically in the tissue of granula-
tions, in tumors of every kind, especially in sarcoma and tubercle. The
giant-cells of bone-tissue, which in later years have been often investi-
gated, are, according to many, metamorphosed osteoblasts, and organs
which dissolve bone-tissue and teeth (osteoclasts). What significance they
possess in the above mentioned new-formations, it is not yet clear : in
many they are found only occasionally, as in granulations, while in many
sarcomata and in all true tubercle their occurrence is constant.

In one other series of cases the nuclei, in endogenous cell-formations,
become in the interior of the cells—probably by a kind of wrinkling of
the cell-contents—cells : so-called MOTHER-CELLS WITH DAUGHTER-CELLS, or
mother-cells with daughter-cells and daughter-nuclei. Finally, the
daughter-nuclei like the daughter-cells, by a rupture of the membrane of
the mother-cell, become free, and the original or mother-cell is destroyed.

The PHYSIOLOGICAL IMPORTANCE of the above-mentioned formations was first
made known by KÖLLIKER (*Würzb. Verh.*, V., 2, March, 1872). Where bones and
teeth depend upon a resorption in the normal course of development, they always
show a finely pitted surface (so-called Howship's lacunæ). In each pit, and corre-
sponding in form and size, there is, for the most part, a giant-cell ; sometimes a
single giant-cell fills two pits ; or larger pits contain many giant-cells. The giant-
cells arise by a transformation of the cells of bone tissue (the osteoblasts), and are
the organs, which dissolve the bone-tissue and teeth : OSTEOCLASTS, (*Knochen-
brecher*) or osteophagi. In the interior of bones there are found lacunæ of resorp-
tion with osteoclasts : closely following the borders of ossification of ossifying car-
tilage ; in the walls of all large medullary spaces of developing bones, etc. In the
external surface : on the dental furrow of embryonal jaws ; at many points of bones
bounding the cranial cavity ; etc. Osteoclasts are found also in the resorption-sur-
faces of the dentine of deciduous teeth, as well as in ivory pegs, which had been
driven into living bone. They belong to the same category of elements as osteo-
blasts. Transitions are found between both forms of cells : osteoclasts at first
isolated, then always more numerous between the osteoblasts may be directly
observed ; if the surfaces of resorption of bones again become surfaces of growth,
osteoblasts succeed the osteoclasts, whence K. concludes to a transformation of the
latter by division into osteoblasts. The resorption of bone and teeth is not preceded
by a solution of the lime salts, as in osteo-malacia : inorganic and organic bases
disappear simultaneously. Likewise there is observed a crumbling of hard struc-
tures before their solution ; the disappearing portions of bones always have sharp
smooth walls, etc.

According to WEGNER (*Berl. med. Ges. Sitzg.*, V. 20, March, 1872 ; *Virch. Arch.*,
1872, LVI., p. 523), when bones disappear in a normal or pathological manner, then
there arises in the vessels of the neighboring tissue, dura mater, periosteum, medul-
lary tissue, etc., a growth of the cellular elements of their walls ; the products of
growth, poly-nuclear cells, are pressed against the part in the form of thick
bodies or very thin plates, are slowly buried in more or less deep pits, lacunæ, of the
bones, whilst they by the pressure of growth induce resorption. If the surfaces
disappear, they then grow in a lateral direction to the surface, meet, unite by oppo-
site processes into net-works, form trabeculated membranes with all transitions to a
continuous membranous layer of a finely granular substance with innumerable
nuclei. Now the affected thin bone-surface has disappeared : myeloplaxes are

developed into vessels, or into fibrous tissue, or perhaps into medullary cells. If the process continues, the same events occur in the vessels now lying superficial to the bones, and so layer after layer enters into insensible resorption.

Consult also the earlier investigations of BREDICHIN (*Med. Ctrlbl.*, 1867, No. 36) and RINDFLEISCH (*Lehrb.*, 1873, p. 550 et seq.).

The pathological importance of giant-cells has not yet been generally established. They are formed sometimes in so small numbers and so inconstantly, that they do not change the character of the new-formed tissue: as in the granulation-tissue of various parts. Sometimes they occur constantly and determine alone or especially the character of the new-formation: as in many sarcomata and in tubercle.

LANGHANS (*Virch. Arch.*, LI., p. 66) has observed contractility and motility in giant-cells.

RINDFLEISCH (*Virch. Arch.*, XXIII., p. 519), in opposition to the usual view that increase of cell-nuclei is a progressive metamorphosis, holds that it is conditionally a step toward destruction of cells. R. could, *e.g.*, by arresting the pulmonary respiration of a frog by a ligature and its cutaneous respiration by immersion in water, transform the well-known uni-nuclear colorless blood-corpuscles into cells resembling pus-corpuscles.

If endogenous formation takes place in cells with double membrane, an external, the capsule, and an internal, the so-called primordial sac, and in cartilage-cells, the external membrane remains unchanged, while the primordial sac is divided once or many times: the cells resulting from this division show sometimes only a single envelope, corresponding to the primordial sac, sometimes the latter secretes later still another external membrane or capsule, while the capsules of the mother-cells gradually blend with the intermediate substance.

Sometimes the nucleus within the cell divides not singly, but at the same time pushes out many bud-like formations, which are finally constricted and further develop in the cell-contents as free nuclei.

As CELL-FORMATION IN NUCLEUS-BEARING PROTOPLASM, RINDFLEISCH (l. c., 1871, p. 55) designates that form, where free nuclei apparently are imbedded in a homogeneous substance, but where by reagents there is made to appear a differentiation of the protoplasm, so that each nucleus belongs to a small round cell. This is the case in granulation-tissue, in many sarcomata and cancers. This is not true of giant-cells.

ENDOGENOUS FREE CELL-FORMATION consists in this, that one or many nuclei are formed, independently of the cell-nucleus, out of the cell-contents in a manner not yet fully known, by means of a kind of partial furrowing, which nuclei afterwards become cells and then abandon the mother-cells. Cells new-formed in this manner are always mucus or pus-corpuscles. Many regard this manner of cell-genesis as not proven: free and endogenously formed cells are according to them migrated cells. (See p. 248.)

According to BIZZOZERO (*Gaz. med. Ital.*, 1871. p. 62), the large forms occurring on epithelial surfaces, which forms contain besides a nucleus, as many as twenty forms similar to pus-corpuscles, so that the latter taken up by the former, are swallowed up (*verschlungen*).

Most cells are capable of increase. The movable and fixed corpuscles in connective tissue of every kind, especially also the adventitia of vessels are most often the points of departure of pathological new-formations, also young bone-corpuscles and cartilage-cells, also epithelial and glandular cells (epithelial cells only in their youngest layers); perhaps (see p. 250) also colorless blood-corpuscles. The same capacity is possessed also, but more rarely, by the endothelial cell of the bloodvessels, and especially by those of the lymphatics, also the nuclei of the capillaries, those of the neurilemma, sarcolemma, and the nuclei of organic muscle-fibres.

Concerning the share which the elements of the walls of the bloodvessels take in new-formations, see VIRCHOW, *Arch.*, XIV., p. 1.—WEBER, *Ib.*, XXIX., p. 84.—SICK, *Ib.*, XXXI., p. 265.—ARNDT, *Ib.*, LI., p. 495.

The uppermost cells of the skin and most mucous membranes, common bone-corpuscles, according to many also the endothelium of serous membranes and vessels, as well as all more greatly degenerated cells, have lost the capacity of increase. Likewise little has been demonstrated with certainty respecting the part taken in cell-formation, of the so-complicated nerve-cells of the ganglia, brain and spinal cord.

RINDFLEISCH (*Lehrb.*, 1 Aufl., p. 221) has taken the view respecting the epithelium of serous membranes, that malignant new-formations proceed directly from it. Consult also RECKLINGHAUSEN on the epithelium of lymph-vessels (*Graefe's Arch. f. Ophthalm.*, 1864, XII., H. 2, p. 62 ; *Sitz.-Ber. d. Würzb. ph.-med. Ges.*, 1865–66.— KOESTER (*Virch. Arch.*, XL., p. 468). According to MEYNERT, processes of division of the bodies of the cortical substance of the brain in febrile diseases (typhoid fever, acute tuberculosis). Likewise according to TIGGES (*Allg. Ztschr. f. Psych.*, XX.).

The youngest new-formed cells are commonly small, round, have for the most part no proper membrane, but a distinct nucleus and nucleolus. In this state they show no further peculiarities from which their later form, size, arrangement, etc., can be determined or conjectured : *i.e.*, those youngest cells, so-called formation-cells, or primordial cells, or granulation-cells, are to be differentiated in the course of their development like the tissues of the embryo ; they may become connective tissue corpuscles, bone-corpuscles, muscle-fibres, etc., or also cancer-cells, sarcoma-cells, etc., and, according to many, also true epithelium ; they may secrete an intercellular substance, which remains always liquid, or later becomes solid, remains homogeneous, or becomes fibrous, etc.

The cells which arise from various tissues usually give rise to definite new-formations : especially true is this of true epithelium, from which only epithelial formations arise (epithelium of regeneration, glandular new-formations, epithelial cancers) ; from connective tissue is developed a connective tissue, poor or rich in cells (cicatricial tissue—fibroma, sarcoma, endothelial and connective-tissue cancer, etc.) ; vessels arise from vessels, etc. Only a number of less characteristic new-formations, especially those formed of nuclei and small cells, may be formed from different tissues, with the exception of true epithelial tissue : thus probably lymphomata, connective-tissue cancers, etc. (Concerning pus-corpuscles, see p. 247.)

Most probably the laws of normal development, which belong to the cells of the three germinal layers and their derivatives, also operate when these cells become subject, in a pathological manner, to formative irritation. Accordingly all pathological epithelial formations are descendants from the cutaneous and glandular layers ; all connective tissue, osseous, vascular, etc., formations arise from the middle blastodermic layer. Genetic mixing of the different cell-forms probably no longer takes place after completion of the separation of the cells in the blastodermic membranes. The endothelium of blood- and lymphatic vessels, of serous membranes, lymph-glands, etc., may again produce endothelium, and probably also connective tissue. According to many, pus-corpuscles may have their origin in the tissues and organs of all three blastodermic layers. (*Vide infra.*)

The TRANSFORMATIONS OF ONE TISSUE INTO ANOTHER, histologically and chemically different, belong properly to the metamorphoses, but may with

propriety be treated of here. These transformations of tissues have many physiological types: thus the transformation of mucous tissue into fatty tissue, that of bone and cartilaginous tissue into connective, or medullary and bone-tissue, etc.

Such tissue-metamorphoses occur PATHOLOGICALLY, in part in epithelial forms, for the most part by the transformation of epithelium of a more or less cylindrical form into pavement epithelium. In part they are found in tissues belonging, in the broadest sense of the word, to connective tissue. Common connective-tissue cells may be transformed into those of mucous, cartilage-, bone-tissue, fat-cells, etc.; common basis substance into mucous, cartilage-, bone-, etc., substance, sometimes with little, sometimes very great difference of chemical composition. A transformation of a connective-tissue substance into a true epithelial one, or *vice versâ*, the latter into the former, has not with certainty been observed.

The GROWTH of hypertrophies and tumors is the same in general as that of normal tissues. It takes place sometimes from the beginning with tolerable uniformity; sometimes it is irregular, even periodical, and for the most part without known cause, rarely dependent upon menstruation, pregnancy, local irritations, general diseases, etc. But in particular, growth is different, according as the new-formations are circumscribed, are diffuse. The former are, with few exceptions, confined to the uterus, while many of the latter may affect promiscuously almost all tissues.

Circumscribed tumors grow by enlargement or increase of their elements; the neighboring parts have no share in the growth, but become simply separated from one another: so-called CONCENTRIC GROWTH. Diffuse or infiltrated new-formations grow partly in the same manner; but especially by the change of layer after layer of the neighboring tissues, in the same manner as at the beginning: EXCENTRIC or PERIPHERIC GROWTH. Sometimes these new-formations, especially tubercle and cancer, develop as new tumors (daughter-tumors) about the first tumor (mother-tumor), which new tumors gradually unite with the former and with one another.

All malignant tumors, those really and those apparently circumscribed, as especially the diffuse, so grow, according to VIRCHOW, that the first tumor, the "mother-tumor," reaches only a small size and afterward ceases to grow. In the meantime, however, new tumors, "daughter-tumors," are formed in its neighborhood, which finally become so large that they come in contact with one another and coalesce with one another and the principal mass. Between them in the periphery new tumors are formed, etc., the daughter-tumors are, according to V., formed by the spreading of an infectious matter, a miasm from the place of the first formation, and indeed by direct imbibition, simple endosmosis, into the neighborhood.

The progress of growth in true and false hypertrophies in general is slow. In tumors it varies greatly.

The LAWS OF THE CIRCULATION AND NUTRITION of hypertrophies and tumors are the same as those of normal parts of the body: therefore not only all the disturbances of circulation (especially anæmia, hyperæmia, and hæmorrhage), but also inflammation and gangrene, as well as almost all disturbances of nutrition (especially simple atrophy, fatty and mucous metamorphosis), and on account of the (for the most part) irregular distribution of vessels, etc., occur comparatively often. All these disturbances of nutrition have an influence with respect to the new-formation itself, often also with respect to the whole organism, since they change the former, even inducing decay, and may exercise upon the latter an influence sometimes beneficial, sometimes injurious.

The most important events of hypertrophies and tumors are therefore:

Unchanged existence (many congenital tumors of the skin, many lipomata and fibromata may remain unchanged for years and tens of years).

Progressive growth, until surgical or medical assistance becomes effective, or death appears.

Disturbances of the circulation, of every kind.

Atrophy and degeneration of almost every kind, especially simple atrophy and fatty metamorphosis, especially important in hypertrophic striated and smooth muscles; regularly in tubercles (so-called yellow tubercle); not rarely in cancers, etc.

Gangrene, mostly dry, very rarely with complete elimination.

Spontaneous retrograde formation: many warts and corns, also pointed and broad condylomata; to a certain degree, almost all cicatrices, bone-callus, almost all syphilomata, many cysts, sarcomata, and carcinomata; general increase of fat in old age.

Transformation of a hypertrophy or new-formation into another new-formation, especially homœoplastic into heteroplastic formations, so-called DEGENERATION: formation of cancer in cicatrices of every kind, in almost all hypertrophies, and in many tumors; sarcomatous formation in fibroma; sarcomatous and cancerous formation in mother-marks, etc. These transformations or degenerations occur sometimes without a known cause, sometimes they are consequences of mechanical or chemical irritations, to which the new-formation is subjected. Among these latter, as affecting external new-formations, are included therapeutic measures of every kind, especially puncture and extirpation.

Differing from this are the so-called COMPOUND or MIXED TUMORS, i.e., those new-formations which from the beginning consist of two or more tissues, which usually occur alone.

After spontaneous, therapeutic, and especially surgical removal (extirpation, etc.), the parts affected remain either free from the new-formation, or the latter returns in the cicatrix or in the neighboring tissues: so-called RELAPSE. The latter is rarely found in encapsuled, hard tumors poor in cells, which have been entirely removed; but, on the other hand, it frequently occurs in tumors infiltrated and rich in cells, especially the sarcomata and cancers. Local relapse has its foundation only in incomplete removal, or in the leaving behind tumors which are perfect or have just begun their growth.

THIERSCH distinguishes the continual, the regionary, and the infectious relapse: the first appears after incomplete extirpation; the second, when the same anatomical changes, which preceded the disease in the original site, occur later also in its neighborhood; the third arises from the penetration of infecting elements into the circulation. According to BILLROTH (Wien, Wochenschr., 1867, No. 72), regionary relapses are perhaps dependent upon inoculation of the elements of tumors into the borders of the wound by the knife of the operator.

The GENERAL SYMPTOMS of hypertrophies and tumors vary.

Hypertrophy shows a general increase of volume (and increase of weight) of the affected part. It exists in solid organs as merely so-called hypertrophy, with retention of the normal form or with the production of greater plumpness (e.g., hypertrophic muscles, hypertrophic bones, so-called splenic tumor). In hollow organs it appears as hypertrophy of different kinds: e.g., in the heart as simple, excentric, and concentric hypertrophy, in the

uterus as so-called infarction, here, as in the stomach, intestine, urinary bladder, mostly with dilatation, more rarely with contraction of the cavity. All true hypertrophies are accompanied mostly by an increased function, which is for the most part easily to be seen in non-muscular organs of every kind, and is of the greatest importance, while in glandular organs it cannot usually be positively demonstrated.

TUMORS are sometimes from beginning to end sharply circumscribed; sometimes they gradually become diffuse; sometimes they are from their earliest appearance diffuse, and in the latter case they pass without distinction into almost all tissues (so-called growing malignant tumors). They grow sometimes slowly (especially the so-called homœoplastic tumors, poor in cells), sometimes remarkably quick (many sarcomata, soft cancers), and in both cases for the most part irregularly and excentrically. Tumors growing on free surfaces or in cavities not infrequently soften and break up: the latter takes place sometimes from without inward (in consequence of too great tension of the skin or mucous membrane), sometimes from within outward (in consequence of previous central softening of the tumor and of the skin or mucous membrane, transformed into their tissue).

The INFLUENCE of hypertrophies and tumors is first on the mother-organ, then on the neighboring parts, and finally on the whole organism.

The influence on the mother-organ consists in its enlargement, mostly with increase of function in true hypertrophies (external muscles, heart, bladder, etc.); in destruction of the affected parts by substitution from infiltrations, by compression by tumor-shaped new-formations, in contractions by new-formations in cavities and canals, etc.

The influence on neighboring parts consists especially in pressure upon them, with all its consequences, lessening their motility, giving rise to disturbances of the circulation, etc.

The resistance of various tissues to new-formations is dependent partly upon the kind of tissue, partly upon whether the new-formation is an hypertrophy or a heteroplasia in form of an infiltration or tumor. In hypertrophies the original parts of tissues exist wholly or in part unchanged. Infiltrated heteroplastic new-formations destroy normal structure in general more quickly and thoroughly, especially on account of the obstructed flow of blood and blastema, while circumscribed tumors are followed for the most part only by a compression of various grades.

The following general propositions apply to the tissues. COMMON CONNECTIVE TISSUE is preserved for the most part a long time, but is usually less waving and less fibrous, but more rigid and homogeneous, its corpuscles become smaller or disappear altogether; or it is destroyed by a kind of softening. BONE-TISSUE suffers either a wasting, or becomes necrotic, or loses its lime-salts, while its fibrous basis substance remains. CARTILAGE resists new-formations comparatively long; various changes of the basis substance and cells, even necrosis, appears for the most part only after great compression or complete infiltration of the perichondrium. ELASTIC TISSUE, and especially the tissues consisting of it (many ligaments, middle coat of the larger arteries, lung-tissue), show the greatest resistance to neoplasms. VESSELS vary in their behavior with new formations, according to their structure and function: often they are destroyed (tubercle), while at other times they are related to the nutrition of the new-formation. Arteries stubbornly resist tumors of every kind; veins are attacked by new-formations much more easily, first and most readily in the adventitia, latest in the intima, if they are not compressed by them. Lymphatic vessels are sometimes compressed by the new-formation, sometimes the latter attacks them. MUSCULAR and NERVOUS tissues, for the most part, with the exception of peripheral nerves long exempt, as well as cellular forms (epidermis, mucous membranes, glands), are usually quickly destroyed.

The INFLUENCE ON THE WHOLE ORGANISM varies greatly not only with the different forms of, but also with the same hypertrophy, and with difficulty admits of a general representation. In some cases it is FAVORABLE: this is true especially of regenerations of some tissues and of many hypertrophies, especially of muscular organs. At other times, hypertrophies and tumors are entirely WITHOUT INFLUENCE: this is true especially of small encapsuled formations in organs less essential to life or in some parts of other organs. Tumors so-called, for the most part exercise an UNFAVORABLE influence on the whole organism. This depends, excepting in the case of the affection already referred to of the womb and neighboring parts, upon the number and size, but especially upon the structure and metamorphoses of the tumors.

Some true and numerical hypertrophies are of beneficial influence on the whole organism, since they are followed by a compensating disappearance of other disturbances: thus hypertrophies of the heart in so-called cardiac insufficiency, those of organic muscle-fibre above contracted points, those of one kidney in atrophy of the other, etc. The, until then, not infrequent latent symptoms of the original affection appear at the time when the hypertrophic tissue or organ suffers disturbances of nutrition.

With respect to structure, new-formations, especially tumors proper, are indifferent proportionately to their approach in their gross and finer structure to the normal tissues of the body, their hardness, vascularity and cell-contents, and the distinctness of their encapsulation. On the other hand, they are important in proportion to the opposite conditions, especially if they are rich in cells, and are more connected with the original tissues.

Metamorphoses of hypertrophies are of harmful influence in those which act compensatorily (most new-formations of muscles, etc.). In tumors they are sometimes advantageous, since they prevent farther growth (calcification, etc.), or cause them to disappear, perhaps even to be completely absorbed (fatty degeneration, etc.), or at least are followed by exhaustion of their infectious properties (mucous metamorphosis); sometimes they are detrimental, as many softenings, gangrene, etc.

New-formations, especially tumors, occur, as already said, sometimes singly, sometimes even in great numbers. In the latter case, the tumor affects either one and the same organ (e.g., myoma of the uterus, cancers of the liver or lungs); or similar organs (e.g., exostoses of different bone, sarcomata of the lymphatics of different parts); or it is seated in different organs. In the latter, not infrequently also in the former case many or multiple new-formations rarely have about the same constitution (many cases of common chronic cancer and the cases of acute cancer). Tumors are commonly found in different organs, especially cancers in a varying condition dependent upon the length of their existence. Those new-formations which are first noticed by the person affected, or which show the most marked changes, which also not infrequently have the greatest volume, are called PRIMARY tumors. New-formations of other neighboring organs in continuous connection therewith are called PROGRESSIVE. All other, and for the most part smaller and young tumors, are called SECONDARY, or METASTATIC. These secondary new-formations are located either in the same organ and tissue near the primary or separated from them. Or, they are located in the corresponding lymph-glands (e.g., in the mesenteric glands in tuberculosis of the intestines, in the axillary glands in mammary cancer). Or, they are located in the tissues and organs connected with the organ of the primary new-formation: e.g., in the intestinal serous membrane in tuberculosis of the mucous membrane, in the pleura in mammary cancer, in the liver in cancer of the stomach and intestines, in the bronchial glands, pleura, and air-passages, not infrequently also the liver, etc., in many cases of pulmonary tuberculosis. Or, finally, they are located in organs which stand

in no relation to the organ of the primary new-formation : *e.g.*, in the kidneys in cancer of the stomach, in the jugular glands in cancer of the uterus. The number of the secondary new-formations is sometimes very small, sometimes extraordinarily great.

The origin of secondary or metastatic new-formations has been explained in various ways. In all cases the primary tumor forms the centre of infection, the secondary tumors are the secondary affections arising therefrom by displacement. In serous membranes where, *e.g.*, besides a primary cancer reaching into the serosa, secondary cancers in varying number may be separated and carried away into other parts and there undergo farther development : this has been more often observed in the peritoneum, more rarely in the pleura. In all other cases the origin of secondary tumors takes place through the blood- and lymph-channel. Here there are again found two possibilities. According to the one view, liquid (without corpuscular elements) travels from the primary new-formation within the fissures of tissues or through the lymph or bloodvessels into the circulation, infects the tissues in the parts affected and induces in them like new-formations. This mode of origin is not to be directly observed ; although many microscopical forms can hardly be otherwise explained. The other view is preferable, that from the primary new-formation CORPUSCULAR ELEMENTS, especially cells, still capable of life and propagation, enter the blood- or lymph-vessels or both, and in the blood- or lymph-current act like emboli, and then become fixed in the capillaries (lymph-glands—liver, lungs), or into the blood-capillaries of other organs and tissues, and here either increase, or the adjacent cells give rise to like new-formations. Both views are sustained by the frequency of secondary new-formations in those organs in which the vessels of the primary new-formation are first of all received (lymph-glands—liver, lungs). The second view is supported by the fact that new-formations rich in cells (enchondromata, sarcomata, carcinomata) not infrequently break through the wall of the lymphatic vessels and veins into them, and here, in the blood- as well as in the lymph-current, they continue to spread. Also by the circumstance, that not only large (visible to the naked eye), but also microscopical tumor-masses have been found, like embolic thrombi in the vessels of lymph-glands, in the vena portae and pulmonary artery ; also the peculiar structure of many secondary cancers of the lymph-glands, agreeing entirely with that of primary cancers ; finally, the analogy with secondary or metastatic abscesses of the same organs.

Consult VIRCHOW, *Ges. Abh.*, 1856, pp. 350 et 551 ; *Die krankh. Geschw.*, 1863, I., p. 33.—O. WEBER, *Virch. Arch.*, 1866, XXXV., p. 501.—LÜCKE, *Ib.*, p. 524.— HIRSCHFELD, *Arch. d. Heilk.*, 1869, X., p. 537.—LAVERAN, *Gaz. hebd.*, VI., No. 33. —FELTZ, *Tr. clin. et exper. des embolies capill.*, 1870.—ACKER, *D. Arch. f. klin. Med.*, 1872, XI., p. 173. In a case reported by ACKER there was found a probable migration of cancer-cells out of the bloodvessels into the alveolar spaces and interstitial tissue of the lungs. Farther special evidence bearing upon this will be furnished during the consideration of the new-formations in question.

Whether the cells carried away with the blood- or lymph-current develop further, or whether they act only as bearers of specific new-formations and serve to create in the adjacent elements the same new-formation (so-called METABOLIC EFFECT), has not heretofore been demonstrated by observation. THIERSCH and WALDEYER defend the former for secondary epithelial cancers, while VIRCHOW, O. WEBER, LÜCKE, KLEBS, and others, assume the latter.

Secondary new-formations may finally arise immediately through the lymphatic vessels, as well as through the excretory gland-ducts. The former is possible in serous membranes, at least in the pleura, where an immediate transfer, *e.g.*, of the cancer-cells of the pulmonary pleura upon the costal pleura has nothing histologically

to oppose it. The latter can occur on the skin and many mucous membranes, where, as in cancer, sometimes the part in contact becomes affected : it would then have an analogy in other forms, *e.g.*, syphilitic diseases of the skin.

Some new-formations, especially cancers and tubercle, those of organs essential to life, or of many organs simultaneously, are in many cases followed by CACHEXIA or DYSCRASIA, especially after a long duration and beginning destruction. This is characterized by the usual phenomena of general chronic anæmia, sometimes rather by those of that which depends upon losses of blood and the humors, sometimes that which is dependent upon a want of nutrition (anæmia of inanition).

The causes of these cachexiæ lie most often in the diminished or arrested function of organs essential to life (cancers of the œsophagus, stomach, intestines, tuberculosis of the last) ; in pain, loss of sleep, etc., and resulting insufficient nutrition, etc. ; in the absorption of the elements of the new-formation into the humors, and consecutive disturbances of organs or of the whole organism ; in the absorption of septic products from out of decaying new formations ; in hæmorrhages ; in other forms of disease consecutive upon the new-formations, etc.

An acute cachexia with a, for the most part, high, more or less typical fever, occurs in some acute lymphoid, especially typhous, new-formations.

The CAUSES OF HYPERTROPHIES AND TUMORS are partly predisposing, partly exciting.

The PREDISPOSING CAUSES are :

1. INHERITANCE : shown especially in the adipose state, tuberculosis, syphiloma, cancer, also in many tumors of connective tissue, cartilage and bone, in warts and cysts. By hereditary transmission new-formations either are present at the time of birth (especially many nævi, multiple tumors of the skin), or they are developed only in the later years of life (obesity, tubercle, cancer).

2. AGE : in general, new-formations, especially tumors proper, are frequent at the age of thirty, still more frequent at fifty. Hypertrophy of the brain, so-called, occurs most often at the age of dentition, hypertrophy of the mammary glands at the time of the development of puberty ; many new-formations, especially many of quick growth, occur almost only in youth (teleangiectasiæ, enchondroma, medullary cancer), others in the middle years of life (fibroma, cysts), others in aged individuals (epithelial cancer), many occur in every age (tubercle, syphiloma, cancer). There are congenital tumors, connected with fœtal development as well as with extra-uterine growth, which proceed from fœtal elements : so-called colloid tumors of the clivus, cysts of the broad ligament, etc., exostoses and enchondromata near to or on the epiphysal cartilages.

FRIEDREICH (*Virch. Arch.*, XXXVI., p. 465) found primary cancer of the liver of a woman thirty-seven years old and at the end of pregnancy, very numerous secondary cancers, etc., of the mamma, uterus, thyroid gland, and in a fœtus prematurely delivered by some weeks, and which died on the sixth day, a cancerous swelling in the skin and subcutaneous tissue over the left patella.

3. SEX : new-formations, on the whole, are of more frequent occurrence in men than in women ; many are more frequent in men (epithelial cancer), others in women (lipoma, fibroma, cysts).

Moulting is not accomplished in birds which have been castrated. Likewise young stags, deprived of their genitals, do not have new horns ; older stags cease to change

them. Male castrates, whose testicles have been removed before puberty, develop no
beard, only a few pudendal hairs, thicker hairs on the head; on the other hand, after
castration after puberty the beard remains, but thinner, to old age.

4. EPIDEMIC AND ENDEMIC conditions are sometimes of undoubted influ-
ence: hypertrophy of the thyroid gland, lymph-glands, tuberculosis, perhaps
also cancer.

5. SPECIAL DISPOSITION OF SOME ORGANS and localities, so-called LOCAL
PREDILECTION: tuberculosis of certain organs and parts of organs (apices of
the lungs, ileum, posterior surface of the larynx, etc.), likewise cancer
(lower lip), uterus, vagina, mamma, pylorus of the stomach, etc.), syphilitic
new-formations, especially in parts of the periosteum and osseous tissue
exposed to mechanical, and perhaps also thermic influences.

The parts affected are either physiologically incompletely developed (articular ex-
tremities of bones, roots of the temporary teeth—milk-glands, uterus, testicles); or
they represent pathologically incomplete tissues (frequency of new-formations in
common cicatrices of soft parts, in bone-callus, in retained testicles); or their nutri-
tion is interrupted by existing diseases (frequency of polypi, warts, tubercles, osteo-
phytes and exostoses in chronic inflammation of skin, mucous membrane, bone).

6. EXCESSIVE PHYSICAL AND MENTAL EXERTION, depressing emotions, bad
social conditions are sometimes causes of tuberculosis and cancer.

7. PREVIOUS DISEASES, e.g., measles, typhoid fever: tuberculosis; catarrhs
of mucous membranes: polypi.

The EXCITING CAUSES are in general all conditions which are followed by an
increased supply of nutritive material through hyperæmia, more rarely by
congestion of blood, or by diminished discharge of lymph.

Increased arterial blood-supply is for the most part followed by increased nutrition.
DONDERS and SNELLEN (l. c.), as well as O. WEBER (*Med. Centr.*, 1864, No. 10),
found that during congestion appearing after section of the cervical sympathetic,
wounds, cauterized parts, etc., healed more quickly than in healthy parts. That also
nævi or affections like nævus (papilloma, etc.) proceed from affections of the nerves,
is shown by the cases recorded by BÄRENSPRUNG (*Ann. der Char.*, 1863, III., 2 H.,
p. 91), GERHARDT (*Jahrb. für Kinderkrkh.*, 1871, IV., p. 270), SIMON (*Arch. für
Dermat. u. Syph.*, 1872, IV., p. 24), etc. JOSEPH (*Arch. f. Anat. Phys.*, etc., 1872,
p. 206) obtained, on the frog, other results concerning the influence of nerves on
nutrition and new-formation: he referred the hyperæmia after nerve-section to a
relaxation of all the soft parts of the leg. If a cock's spur be transplanted from
the leg to the comb, where it meets with a tissue much more vascular and receives
a more abundant nutrition, it will often grow excessively (to 12 cent.: PAGET). In
large, slowly growing tumors of the extremities, the hair and nails become enormous,
the vessels, and not infrequently also the nerves, become hypertrophic. In necrosis
in young persons the bones of the extremities have been observed to become longer
(PAGET, STANLEY, O. WEBER), etc.

1. INCREASED FUNCTION: hypertrophy of muscles of every kind, e.g.,
hypertrophy of all the muscles of the body and extremities in laborers,
gymnasts, etc.; of the muscles of the right extremity of smiths, etc.; of the
muscles of the calf of the leg of dancers, etc.; hypertrophy of the heart
from all causes, which continuously or repeatedly increase the heart's func-
tion (abnormal dilatation of the heart, contraction of the valvular orifices,
obstructions in the aorta or pulmonary artery); hypertrophy of the urinary
bladder from obstruction to the evacuation of the urine, that of the stomach
and intestine above constricted points, etc.

Diminished function, especially motion, not infrequently leads to obesity.

2. MECHANICAL (pressure, etc.) AND CHEMICAL IRRITATIONS, especially if they are frequently repeated and if they are of moderate intensity : hypertrophies of the skin (corns, warts, condylomata, etc.), of the mucous membranes, bones, many glands, especially lymph-glands ; formation of pus, granulations, cicatricial tissue ; encapsuling of foreign bodies ; epithelial cancer of the lower lip ; cancer of the tongue and œsophagus, granular liver in drinkers ; so-called *post mortem* tubercles on the hands, especially on the dorsal surface of those of anatomists ; tumors in retained testicles, in cicatrices.

That herein the activity of cells may be independent of the vessels is shown by experiments on plants, and on those lower animals which consist only of cells : the cells as such first of all react to the irritant. Local irritation is insisted upon, by VIRCHOW especially, as essential in the origin of tumors.

How differently the same cause acts upon different persons is shown by the so-called corpse-tubercle : many anatomists, and others, become sick within a few weeks after exposure, others remain entirely exempt. I knew a furrier, who in his stay in his establishment opened the bodies and removed the organs from their cavities : after seven months' labor, and forty-two autopsies, both hands were covered with numerous tubercles, which reached the size of many square inches ; they remained unchanged for three years, when the man resumed his work.

3. VICARIOUS FUNCTION : hypertrophy of the remaining bone in extremities with two bones ; hypertrophy of one kidney, one testicle, after destruction of the other organ ; hypertrophy of lymph-glands in atrophy of the spleen ; etc.

4. POISONS OF DISEASE : small-pox, gonorrhœa, syphilis, glanders, typhoid fever, etc.

These poisons show at the same time, that specific poisons excite a specific cell-activity, which at first appears to be wholly independent of the vessels and nerves.

5. TRANSMISSIBILITY OF A NEW-FORMATION from man to man, as well as that from man to animals and *vice versa*, has until now been demonstrated only of the above-mentioned, for the most part acute and cellular new-formations, as well as of tubercles. Clinical and experimental proofs of the transmissibility of cancer are still wanting.

The experiments of LANGENBECK, LEBERT, and FOLLIN certainly are not conclusive. On the other hand, O. WEBER (*Chir. Erf.*, p. 289) saw in a dog and in a cat a growth like medullary cancer arise after introduction of a moderate quantity of the same under the skin, which sustains the view of direct continuous growth of inoculated cells.

All the above-mentioned predisposing and exciting causes hold good only of primary new-formations and tumors. That other conditions of origin of secondary new-formations exist, has been already mentioned.

Many hypertrophies however, and most tumors are spontaneous, *i.e.*, we do not know the causes of their origin.

The causes of the immunity of many tissues and organs (cartilage, thyroid gland, ovaries) from most, or some new-formations are wholly unknown.

The NOMENCLATURE OF NEW-FORMATIONS is in part so old, that the original sense of the name is now entirely forgotten (*e.g.*, in tubercle, cancer, sarcoma) ; it is in part histological (epithelioma, myoma, neuroma) ; in part ætiological (syphiloma). Compound new-formations are mostly

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named from a part of their structure, that which is most prominent : *e.g.*, adenoma, myoma, enchondroma.

The CLASSIFICATION OF NEW-FORMATIONS may be regarded from various stand-points. The distinction of benign and malignant new-formations is practically the most important. Their classification according to their histological elements, their genesis, the duration of their constituents has not as yet been strictly made.

The INNOCENCE and MALIGNITY of new-formations are purely clinical notions, not at all, or only partly pathologico-anatomical. Those new-formations are in general called malignant, which are almost always, at least in the earlier stages, rich in cells, and therefore soft and often vascular, which extend for the most part without sharp limits into the neighboring tissues, which usually return in the same spot after extirpation, and where for the most part the corresponding lymph-glands, not infrequently also internal organs (oftenest the lungs or liver, sometimes also other organs) become affected in the same manner, and which, finally, by long continuance are attended by sympathy of the whole body (so-called dyscrasia). Danger to life does not depend entirely upon the malignancy of the new-formation : innocent new-formations may likewise be attended with a fatal termination from compression of organs essential to life.

Nothing further need be added with respect to the histological classification of new-formations.

With respect to GENESIS, new-formations are those which are derived from the upper and lower germinal layers (especially epithelial new-formations), those which are derived from the middle layer (on the one hand vessels, on the other connective tissue, etc.), and those which are derived from the latter and one of the former.

With respect to the DURATION OF THEIR ELEMENTS, new-formations are: *a.* transitory (lymphatic new-formation, many tubercles, many cancers, etc.); *b.* permanent (almost all consisting of cells and intercellular substance); *c.* mixed (healing by second intention, many cancers, etc.).

VIRCHOW divides tumors in general into : 1. those which are from the elements of the blood, extravasation and exudation tumors (blood-tumors or hæmatomata ; transudative or exudative tumors, hygromata); 2. those which consist of secreted matters, dilatation or retention-tumors (atheroma, mucous cysts, etc.); 3. those, which proceed from proliferation, proliferation tumors, pseudoplasms, growths.

The classification followed by us, of new-formations, is chiefly a histological one, and, corresponding to practical needs, is at the same time ætiological and clinical.

I. NEW-FORMATION OF CONNECTIVE TISSUE AND OF VESSELS.

New-formations of connective tissue and of vessels almost always occur together, so that a separate consideration of these is admissible in only a few cases.

CRUVEILHIER, *Anat. path.*, 1830, Livr. XXIII., Pl. 3 et 4 ; Livr. XXX., Pl. 5.—SCHWANN, *Microsc. Unters. üb. d. Uebereinst.*, etc., 1839.—HENLE, *Allg. Anat.*, 1841.—HOPPE, *Virch. Arch.*, 1853, V., p. 170.—JOS. MEYER, *Ann. d. Berl. Char.*, 1853, IV., p. 41.—VIRCHOW, *Arch.*, 1853, V., p. 590 ; VI., p. 525 ; XI., p. 287 ; XVI., p. 1 ; *Würzb. Verh.*, I., p. 143 ; II., pp. 150 et 314 ; *Die krankh. Geschw.*, 1863, I., p. 287 ; III., 1 H., p. 306.—SCHUH, *Ztschr. d. Ges. d. Wien. Aerzte*, 1853, p. 481.—ROKITANSKY, *Ztschr. d. Ges. d. Wien. Aerzte*, 1854, p. 256 ; *Lehrb. der path. Anatomie*, 1855.—BILLROTH, *Virch. Arch.*, 1855, VIII., p. 260 ; *Beitr.*, 1858, p. 1.—VERNEUIL, *Gaz. méd. de Paris*, 1856, Nos. 5-8.—*Schm.'s Jahrb.*, B. 91, p. 21.—HESCHL, *Prag. Vjhrschr.*, 1856, XIII.—BAUR, *Die Entwickelung der Bindesubstanz.*, 1858.—B. SCHULZ, *De ortu vas. sanguiferorum*, Bonn, 1860.—O. WEBER, *Virch. Arch.*, 1860, XIII., p. 74 ; XV., p. 465 ; XXIX., p. 84.—L. PORTA, *Dell' angectasia*, 1861.—RECKLINGHAUSEN, *Virch. Arch.*, 1863, XXVIII., p. 157.—KÜHNE, *Unters. üb. d. Protopl. u. d. Contract.*, 1864.—THIERSCH, *In Pitha u. Billroth's Chir.*, 1867, I., 2 Abth., p. 529.—KREMIANSKY, *Wien. med. Wschr.*, 1868, No. 1-6.—RANVIER, *Journ. d. l'anat. et de physiol.*, 1868, II., p. 471.—SCHWEIGGER-SEIDEL, *Arb. aus d. phys. Anst. zu Leipzig.*, 1869, p. 121.—BOLL, *Arch. f. micr. Anat.*, 1871, VII., p.

I. NEW-FORMATION OF CONNECTIVE TISSUE.

New-formed connective tissue occurs under three forms: as regeneration
of connective tissue or as cicatricial tissue,—as so-called connective tissue
hypertrophy or induration,—and as connective-tissue tumor.

A new-formation of connective tissue occurs PHYSIOLOGICALLY, in various physio-
logical hypertrophies of the skin, fat-tissue, muscles, tendons, fasciæ, ligaments,
bones, etc., arising chiefly from increased function, and in the healing of physio-
logical hæmorrhages (umbilical cord, uterine mucous membrane, ovaries).

COMMON or FIBROUS (fibrillar) CONNECTIVE TISSUE is oftenest new-formed.
It consists of unbranched CONNECTIVE-TISSUE FIBRILLÆ, which yield gela-
tine, which are sometimes arranged in bundles (CONNECTIVE TISSUE-BUNDLES),
sometimes irregularly or regularly, and which are more or less loosely
interlaced (NET-LIKE and COMPACT CONNECTIVE TISSUE). Finally, it is
either SOLID, so-called FORMED, as in tendons, serous, fibrous membranes,
the corium of the skin and mucous membranes, the periosteum, cornea,
etc., or it is LOOSE, AREOLAR, so-called FORMLESS, as in fat-tissue, between
the intestines, muscles, etc. Between the connective-tissue fibres and
bundles there is everywhere found a minute or more abundant quantity of
fluid, formless, albuminous substance, the so-called INTERMEDIATE SUB-
STANCE, or CEMENT.

His denies the existence of the intermediate spaces of loose connective tissue
except in the sub-arachnoid spaces, as well as between the sclera and choroid. All
remaining spaces of connective tissue are, according to H., either lymphatic capil-
laries, or they are filled by so-called mucous or mucoid substance, which with the
fibrous substance, H. considers as an essential element of connective tissue.

Two different kinds of corpuscles are found in connective tissue. With-
out preparation (or after the addition of acetic acid, etc., whereby the
fibres swell and become very pale) there appear corpuscles in varying
numbers, which serve not only for the movement of the juices and the
nutrition of the connective tissue, but also are of especial importance with
respect to the development of most new-formations. They are, according
to the older view, either small, slender nuclei not connected with one
another (so-called connective-tissue nuclei), or larger, spindle or star-shaped
cells with distinct nucleus and with two or more filamentous, for the most
part hollow processes: CONNECTIVE-TISSUE CELLS or CONNECTIVE TISSUE COR-
PUSCLES. According to the more recent investigations these bodies are
mostly elongated, irregularly dentated, in different localities and in differ-
ent ages in various parts variously formed crooked plates, which contain,
centrally or excentrically, a smooth elliptical nucleus and about this, granu-
lar protoplasm: CONNECTIVE-TISSUE CELL-PLATES. Besides, connective
tissue in many places contains a second form of corpuscles, which have the
same size, the same optical properties, the same contractility and ability to
wander, as colorless blood-corpuscles and pus-corpuscles. They are dis-
tinguished from the first described variety, by the designation: movable
connective-tissue corpuscles, or wandering cells. They originate most

probably in the blood. Their signification is not yet known. We little know likewise, whether one kind of connective-tissue corpuscles can pass by transformation into another.

A greater part of connective tissue corpuscles have, by the more recent investigations of tendons by RANVIER and BOLL, of the cornea by SCHWEIGGER-SEIDEL and BOLL, of other forms of connective tissue by FLEMMING (see new-formation of fatty tumor), shown a compound structure. Accordingly the nucleus and the dark protoplasm surrounding it, which alone has hitherto been regarded as connective-tissue corpuscles, lie in the centre or periphery of a large, elongated, irregularly dentated, variously curved plate. These plates (BOLL's endothelioid cells) probably communicate regularly by means of very delicate, easily broken, pale processes. The protoplasmic contents fluctuates with the form of the plate: it is least in especially flattened cell-forms, while rounded cell-forms (e.g., in the stroma of the testicle) have a distinctly granular protoplasm. According to BOLL connective-tissue cells are not always bound to fibrillar connective tissue, but occur also independently, as in the testicle, where they lie immediately upon the walls of the capillary vessels. In most flattened forms the individual independence of the cells is lost, and their limits become invisible, so that extended membranes finally appear, whose cellular composition can no longer be seen, but only inferred. The plates line the clefts in connective tissue and cornea, and in this relation act like the endothelia of lymphatic vessels and serous membranes. According to RANVIER, every single cell-plate is rolled up into a hollow cylinder and is firmly united with neighboring plates, so that there is formed a kind of drain-pipe: the connective tissue therefore is a lymph-sac. According to FLEMMING, it is a system of lymphatic spongy cavities, whose walls consist of fibrillæ and an interfibrillar substance; the above cells are located on the latter like interrupted endothelium. In tendons, the cells lie so near to one another, that there is formed by them a branched system of endothelial tubes, a plasmatic canal system (RANVIER). According to BOLL, investigation of embryonic tendons shows, that the cell-plates sheathe the fibrillar bundles themselves; they are themselves parts of the elastic sheaths of the connective-tissue bundles.

The channels in which migratory connective-tissue corpuscles move, are not yet certainly known: they are either the circumscribed spaces of connective tissue plates, or it is the cement between the fibrillæ. Some connective-tissue cells with processes of various length and thickness, with finely granular contents, with distinct oval nucleus or nucleus-like body, show a slow change of form, but no change of locality.

HOMOGENEOUS, or REICHERT'S CONNECTIVE TISSUE is rarely new-formed. It contains no distinct bundles or fibrillæ, but consists of a substance, which is membranous with respect to extent, or exists in large masses, is finely granular or slightly striated, wholly homogeneous, clear and which probably likewise furnishes gelatine. It is found in so-called homogeneous connective-tissue membranes (the bright sheaths about the bundles of the arachnoid, the adventitia of smaller bloodvessels, the neurilemma of smaller nerve-branches, the envelopes of the Malpighian bodies of the spleen, gland follicles of the intestine, the envelopes of the glandular elements of the testicles, Graafian follicles, many racemose and pouch-shaped glands).

Manifold transitions are found between fibrillar and homogeneous connective tissue.

The so-called MUCOUS TISSUE or GELATINOUS CONNECTIVE TISSUE, which occurs in the vitreous body, Wharton's jelly of the umbilical cord, in the foetus in place of fat-tissue in medulla, etc., consists of a mucus-like basis substance containing mucus and albumen, not yielding gelatine, sometimes provided with round, partly amœboid, sometimes with radiate, anastomosing, soft, nucleated cells.

New-formed connective tissue of every kind almost always contains bloodvessels; for the most part also lymphatics, sometimes nerves.

New-formation of pathological connective tissue takes place, according to the views held heretofore, from connective tissue itself in all its varieties. By division of the connective-tissue corpuscles, more rarely by endogenous new formation, there arise sometimes only two cells, sometimes a mass of cells, which either are spindle-shaped (so-called spindle-shaped connective-tissue cells), or which at the beginning have a round form, but immediately become spindle-shaped or radiate. How basis substance arises between these cells (FIBRO-BLASTS), lying at first in close opposition, has not yet been with certainty observed. According to one view, it arises by direct metamorphosis of the protoplasm. According to another view, the cells secrete a soft homogeneous substance, which either always remains soft and homogeneous, contains mucus and albumen (mucous tissue), or it obtains a greater consistence (homogeneous connective tissue), or hard and affording gelatine, becomes fibrillar (fibrous or common connective tissue). The cells, if their basis substance is formed, rarely retain their distinctly cellular nature, but become afterward for the most part more indistinct. (Or they are further transformed into fat, pigment-cells, etc.) The basis substance may in time undergo various changes. According to some, also the formative cells of connective tissue are in many cases migrated colorless blood-corpuscles: at least they are like them in all points, contain coloring matters, which had previously been injected into the animals, and migrate in oval and spindle-shaped cells and further on into fibrous tissue.

NEUMANN (*Arch. d. Heilk*, 1869, X., p. 601) himself concludes with respect to pathological new-formation of connective tissue (SCHWANN'S and BEALE'S view), that the protoplasm of cellular elements is metamorphosed into fibrillar connective tissue intercellular substance. The cells in this metamorphosis are called "FIBRO-BLASTS." W. KRAUSE (*Deutsche Klin.*, 1871, No. 20) regards connective tissue fibrillæ as cell-processes, not as intercellular substance. According to M. SCHUTZE (see BOLL, l. c.), a direct metamorphosis of protoplasm into fibrillar substance does not take place, but the latter is something new like cellulose, fat, starch.

According to SCHEDE (*Arch. f. klin. Chir.*, 1872, XV., p. 14) after a single energetic pencilling of the skin of a rabbit with tincture of iodine, the emigrated cells become greater from day to day, their form becomes like that of old connective-tissue corpuscles, and on the fifth or sixth day most of the migrated corpuscles are completely metamorphosed into connective-tissue corpuscles. Others go back unchanged into the lymphatics. The old fixed connective tissue corpuscles therein show no change. Fatty metamorphosis begins on the fifth or sixth day in the old connective-tissue cells and then also in the younger less developed migratory cells. Farther on are found all stages of transformation of common connective-tissue corpuscles into fat-cells (FLEMMING). Some connective-tissue fibrillæ are probably also destroyed. Finally, the previous status is restored. According to SCHEDE, iodine tincture causes only an acute increase of normal physiological processes.

Connective tissue probably arises in the first described manner from cartilaginous tissue and from young bone-tissue; also from other tissues not immediately belonging to it: *e.g.*, from the capillaries, transversely striated muscle- and nerve-fibres, where their nuclei afford the starting-point of increase, from the so-called membrana propria of glands.

In the blood-coagula of vessels and in hæmorrhages of every kind, especially also in blood-filled wounds, the starting-point of connective-tissue formation is the endothelium of vessels, also the cells of the other tunics of the vessels, etc., and, according to many, the colorless blood-corpuscles. (See p. 192.)

SPERLING (*Ctrlbl.*, 1871, No. 29) injected the fresh coagulable blood of rabbits between the dura mater and arachnoid of the same animals. After eight days, this blood

showed the beginning of an organization into a connective-tissue membrane, which after from two to three weeks was perfected ; after three weeks, the vessels also were new-formed. The membranes resembled those of hæmorrhagic pachymeningitis. The organization of the blood took place on the convex surface of the brain, on the inner surface of the dura without adhesion to the arachnoid. The membrane was formed from the fibrin contained in the injected blood. After injection of defibrinated rabbit's blood, there occurred no new-formation of membrane, but the blood was wholly or in great part absorbed.

Mucous tissue is sometimes formed at first, and is later transformed into a substance similar to homogeneous and fibrous connective tissue.

Finally, there occurs a pathological new-formation, which is founded on a TRANSFORMATION of various normal tissues : so-called FIBROUS METAMORPHOSIS. This occurs most often and prominently in many chronic inflammations of joints. Fibrous connective tissue, short or long, arises by transformation of cartilage-cells into connective tissue cells, and by fibrillation of hyaline cartilaginous basis substance. A substance, more or less like connective tissue, is formed in many inflammations of bone after absorption of the normal bone-salts from the bone-tissue. Finally, by the disappearance of the proper contents of transversely striated muscle-fibres, nerve-fibres, glandular organs and vessels, the surrounding envelope splits and later becomes fibrous ; normally, the corpuscles, nuclei, etc., occurring in the envelope (capillary wall, sarcolemma, etc.), are either at the same time destroyed, or they remain permanent as connective-tissue corpuscles.

Likewise as fat-tissue arises from mucous tissue, so fat-tissue not infrequently again becomes mucous tissue, especially in states of emaciation : in sub-pericardial fat-tissue, in the fat in the hilus of the kidneys, about the spinal dura mater, in the medulla of tubular bones, etc.

2. NEW-FORMATION OF VESSELS.

The new-formation of vessels affects in part only bloodvessels, most often the capillaries, more rarely small arteries, almost never larger arteries and veins ; and in part lymphatic vessels.

Not only an elongation and dilatation of pre-existing vessels occurs PHYSIOLOGICALLY in the pregnant uterus, by increase of wall-elements, but also a formation of new vessels.

NEW-FORMATION OF BLOODVESSELS occurs most frequently at the same time with new-formation of other tissues, especially of connective, bony, and muscular tissue. New-formation of vessels is thus found during healing of wounds, especially distinct in so-called granulations, also in pseudo-membranes, and adhesions of serous membranes, in true and false, partial and general hypertrophies of most tissues and organs, also of the decidua vera (so-called *placentæ spuriæ*), in almost all tumors.

Vessels occur more rarely as the only or chief new-formed tissue. This is on the one hand the case in the formation of so-called COLLATERAL CIRCULATION, on the other hand in vascular tumor. Concerning the former, see p. 174. VASCULAR TUMOR, ANGIOMA, is a new-formation, which has a more or less distinct tumor-like outline and consists for the most part or almost wholly of vessels. Most tumors may at any period of their existence, in some parts or for the greatest part, become very vascular. This condition is termed CAVERNOUS or TELEANGIECTATIC DEGENERATION (fibroma

teleangieetodes, enehondroma tel., ete.), or it receives special names, *e.g.*, fungus hæmatodes.

The vessels in collateral circulation and in new-formations are in part the very elongated and dilated small arteries, veins, and capillaries of the organ, in part, especially in the latter, they are new-formed, and then they are distinguished from normal vessels by their considerable lumen, by their irregularity (in places varicose or aneurismal) and by some less important anomalies of structure, especially the greater thinness of their walls.

The BLOOD in new-formed vessels always flows from the original vessels of the body into them, is never new-formed.

CARMALT and STRICKER (*Oestr. med. Jahrb.*, 1871, p. 428) have only recently observed in the inflamed corneæ of the frog and rabbit a new-formation not only of bloodvessels, but also of blood.

NEW-FORMATION OF VESSELS, especially of the CAPILLARIES, ensues in various ways.

a. By INTUSSUSCEPTION, like normal growth : vessels of every calibre, especially often smaller arteries and veins as well as capillaries, become longer, tortuous and dilated (eirsoid or serpentine ectasia). The tissue-elements of their wall increase in size or also in number. The capillary vessels thus elongated sometimes finally communicate in a still unknown manner. This process occurs in the formation of collateral circulation, as well as in hypertrophic organs, not infrequently also in the base of pedicled tumors, or in all the surrounding tissues of new-formations.

b. By BUDDING : here again are found two different forms :

α. Buds shoot out from the smallest arteries or capillaries, which buds have a broad base and pointed extremity, are at first SOLID, then become hollow and finally communicate with like sprouts of other capillaries, more rarely with the latter without the intervention of sprouts. According to more recent investigations, a germinative protoplasm is produced from the cells of the endothelial pouch of developed vessels, by whose growth buds and filaments are formed, which by the coalescence of their proto-plasma-granules are transformed into cords. By liquefaction of the central mass of this protoplasm, protoplasma-tubes are formed, which by further metamorphosis of the wall, *i.e.*, nuclear formation in it, by segmentation of the granular mass about the latter, etc., are transformed into tubes built up of nuclear bodies, and finally into sacks composed of nuclear plates.

β. Or there occurs in the connective tissue in the vicinity of the capillaries a repeated division of connective-tissue corpuscles ; thereby cellular cords are formed, which finally, with the exception of the most external cells which are transformed into the vessel-wall, become hollow and communicate with vessels : frequent in granulations.

c. By CONNECTIVE TISSUE CORPUSCLES BECOMING HOLLOW :· spindle-shaped and radiate connective-tissue corpuscles dilate and are transformed into canals, which unite with other connective-tissue corpuscles and finally with vessels, sometimes by means of the budding described above.

d. Vessels in wounded parts, capillaries as well as arteries and veins, are transformed into SOLID CELLULAR cords, channels arise between the new-formed cells, which at first are permeable ONLY FOR BLOOD-PLASMA ; most of these channels disappear, while the remainder, by blending, etc., of the cells bounding the channels, become PERMANENT VESSELS.

The first mode of new-formation of vessels has been longest known; the second

was demonstrated by Jos. MEYER. the third by SCHWANN, REMAK and others, the last by THIERSCH. QUEKETT, TRAVERS, PAGET and others have assumed still other forms of new-formation of vessels.

According to RANVIER (*Nouv. dict.*, etc.). every pathological new-formation of vessels depends upon a growth of the endothelia of the capillaries, which under the influence of the inflammation, etc., have reverted to the embryonic state.

ARNOLD (l. c.) investigated the development of blood-capillaries in amputated tails of tadpoles. in process of regeneration. in inflamed corneæ of rabbits and guinea-pigs, and in the embryonic vitreous. The development of capillaries always proceeds from a vessel already present. It begins with the accumulation of granules, which arrange themselves into rows and by increased accumulation of protoplasm are transformed into smaller or larger forms, the SHOOTS. These increase in length and breadth. By their advance in the direction of their length the shoots become PROTOPLASMA-FILAMENTS. The advance takes place within the brighter channels, which perhaps correspond to the connective-tissue fissures. By the combination of the most external rows of two protoplasma-cords, etc., there are formed the PROTO-PLASMA-ARCHES. Canalization occurs by solution of the central protoplasm in form of molecules and larger particles, which are still demonstrable for a long time in the circulation. The metamorphosis of the original homogeneous protoplasm-tube into the endothelial cell tube is regarded by A. as a kind of segmenting process of the protoplasm. The remains of protoplasm remaining between the cells form the so-called cement The adventitia of vessels is formed altogether independently of the endothelial sac, probably out of the spindle-shaped cells of the basis substance. From ten to twelve hours are necessary for the complete development of a capillary tube of medium size in the tail of a tadpole. Even solid or incompletely canalized shoots, cords, and arches, are formed also from new-formed vessels as well as from those originally present.

The smaller ARTERIES and VEINS are most frequently formed by transformation of already present or new-formed capillaries, while cells are also formed by division, etc., surrounding the vessels and finally pass over into the various tissues of the coats of the vessels. More rarely larger vessels of the same kind are also formed primarily from solid cellular cords.

In many tumors of luxurious growth, also in simple chronic processes of growth, vessels are found of the width of small arteries, but without muscles, their walls being formed exclusively of numerous layers of spindle-shaped cells. (KLEBS, *Virch. Arch.*, XXXVIII., p. 210.)

The ARRANGEMENT OF NEW-FORMED VESSELS sometimes offers no special abnormality, while it is analogous to that of the mother-tissue; sometimes there are peculiar conditions. Thus in many new-formations there occur proportionately long, simple clubs, which may sometimes dilate, cyst-like, and separate. In many pseudo-membranes of serous membranes there are found the so-called bi-polar *rete mirabile*, etc.

NEW-FORMATION OF LYMPHATIC VESSELS has with certainty been demonstrated in only few cases, but it probably occurs very often. The immediate processes are unknown: probably they are formed like the blood-capillaries as intercellular ducts.

Cases of new-formation of lymphatic vessels were observed by SCHRÖDER V. D. KOLK (LESPINASSE, *De vas. pseudom.*, 1842), and TEICHMANN. in pseudo-membranes, by the author on the pulmonary pleura (*Arch. f. phys. Heilk.*, 1859, p. 343). According to KRAUSE (*Ztschr. f. rat. Med.*, 1863, XVIII., p. 263), the lymphatics in many tumors are injected: in cancer, they course in the connective-tissue framework of the stroma.

A. NEW-FORMATION OF VASCULAR CONNECTIVE TISSUE AS REGENERATION OR AS CICATRICIAL TISSUE (HEALING OF WOUNDS, CAPSULE-FORMATION, ETC.).

HUNTER, *A Treatise on the Blood, Inflammation, Gun-shot Wounds*, etc. Phila.,

1796.—REDFERN, *Monthly Journ. of Med. Sc.*, Sept., 1851.—STRUBE, *Der norm. Bau d. Cornea u. die path. Abw.*, 1851.—THIERFELDER, *De regen. tendin.*, 1852.—HIS, *Beitr. z. norm. u. path. Hist. d. Hornhaut*, 1856.—ADAMS, *On the Repair. Proc. in Hum. Tendons*, 1860.—LEIDESDORF and STRICKER, *Wien. Sitzgsb.*, 1866.—HOLM (-STRICK-ER), *Ib.*, 1867, LV., p. 493.—WYWODZOFF, *Oestr. Jahrb.*, 1867, p. 3.—COHNHEIM, *Virch. Arch.*, 1867, XL., p. 1.—THIERSCH (l. c.).—AUFRECHT, *Virch. Arch*, 1868, XLIV., p. 180.—GÜTERBOCK, *Ib.*, 1872, LVI., p. 352.—PAGET, *Surg. Pathol.*, p. 144.

In organs which consist only of connective tissue, or of this and of vessels, as well as in numerous other organs consisting in part or chiefly of other tissues, connective tissue, which is almost always vascular, is new-formed after wounds, ulceration, and losses of substance of every kind. This new-formation takes place in two different ways, which histologically show slight differences, but clinically have been for a long time distinguished as so-called HEALING BY FIRST, and HEALING BY SECOND INTENTION. In the first case, union of the borders of the wound takes place by new-formation of connective tissue and vessels, IN THE SHORTEST TIME AND WITHOUT FORMATION OF PUS. In the other case, likewise, connective tissue with vessels is formed, mostly in shape of so-called GRANULATIONS, which finally, after shorter or longer times, brings about union, with the formation of a more distinct cicatrix ; besides, PUS is here formed in varying quantity, which flows off or is destroyed, and has nothing to do with healing itself. Sometimes healing occurs in one and the same wound by both first and second intention simultaneously ; the one at one point, the other at another point in the long diameter of the wound ; or the one superficially, the other deeply.

In both forms of healing, so-called CONGESTIVE HYPERÆMIA is found in the vicinity of the wound : this is in part of collateral origin, in part it appears (in parts supplied with sensory nerves) in consequence of a reflex paralysis of the vaso-motor nerves.

Healing of wounds behaves differently, according as it occurs in non-vascular or vascular parts.

a. HEALING OF WOUNDS IN NON-VASCULAR PARTS.

This mode of healing has, experimentally as well as clinically, especially in the cornea, often been investigated ; nevertheless the theories with regard to it are at the present time very widely divergent.

In WOUNDS OF THE CORNEA (traumatic, wounds from cauterization), especially of the centre of the cornea, there is formed around the wound, after a few hours, a narrow whitish, milk-colored circle, the corneal border and the conjunctiva early become hyperæmic, finally œdematous. The portion of cornea nearest the injury is likewise clouded. This cloudiness points in the direction of the wound, and after from one to three days reaches it. While the cloudiness around the corneal wound becomes deeper, the periphery clears up again, and after from three to seven days is perfectly clear. This cloudiness around the cornea depends, according to the older theory, upon an increase of corneal corpuscles ; according to the more recent view, especially that based on the so-called feeding of colorless blood-corpuscles with coloring matters, it depends upon migrated corpuscles (pus-corpuscles).

According to the old view, whose representatives are STRUBE (1851), with VIR-CHOW, HIS (1856), LANGHANS, and many others, a growth of the nucleus of the corneal corpuscles appears after eighteen hours, in the proper cell-body as well as in the cell-processes. These new-formed nuclei and cells become connective tissue, if the

healing is by first intention.   Otherwise, especially in sloughing from cauterization, pus appears and new vessels are formed from the corneal border, until finally healing is accomplished in the usual manner.   Normal corneal tissue is rarely formed in both cases in man; for the most part there remains a clouded, less transparent spot, a so-called OPACITY OF THE CORNEA.

The more recent views are by RECKLINGHAUSEN, HOFFMANN, COHNHEIM, and A. KEY, for which see p. 251 *et seq.*   Consult also GÜTTERBOCK (*Virch. Arch.*, L., p. 465). He found in healing by first intention in both borders of the wound in the cornea, from five to seventy-two hours after the injury, numerous spindle-shaped elements, arranged perpendicularly to the borders of the wound and parallel to one another. These, in part, are metamorphosed branched corneal cells.

Concerning WOUNDS OF CARTILAGE, *vide infra.*

b. HEALING OF WOUNDS IN VASCULAR PARTS.

In the healing of wounds of vascular parts, *e.g.*, of the skin, by FIRST INTENTION, the processes appear in the following manner.

a. In many cases there is only very slight hæmorrhage, as in many purely incised wounds of the skin.   The surfaces of the wounds are glued together by an albuminous liquid which is never visible on the surface, but is infiltrated into their deeper layers.   This adhesion is followed after a few days by complete union.   The borders of the wound never show redness and swelling; the wound pains only at the moment of reception and for a little time thereafter.   No cicatrix is formed.   This mode of healing is designated by the term IMMEDIATE UNION.   The processes microscopically are the same as those of the following mode.

Consult thereon MACARTNEY (*Treatise on Inflammation*), PAGET, and THIERSCH. GUSSENBAUER (*Arch. f. klin. Chir.*, 1871, XII., p. 791), from experiments on the cornea, cartilage, etc., denies the existence of so-called immediate union.   The surfaces of wounds do not adhere immediately, but by an intermediate substance, which is coagulated, or coagulable tissue-fluid: in the cornea, its parenchymatous juice; in cartilage, blood and tissue-fluid; in other tissues, blood and interstitial tissue-fluid. This intermediate substance occasions the first new connection of the tissues.   Then is added exudation.

β. In healing by FIRST INTENTION proper, the bleeding of the wound-surfaces is greater.   After this has ceased from the larger wounded vessels, still a slight hæmorrhage from the smallest vessels remains.   The blood, in part, runs off, a portion collects in the wound, some is infiltrated into the surrounding parts. The blood coagulates in these places, and thereby partly effects a cementing of the borders of the wound together.   But for the most part the closure is effected by a liquid rich in albumen infiltrating the wound-surfaces.   If the hæmorrhage ceases, the wound appears moist, and lets an albuminous liquid escape; but motion, etc., causes it to bleed easily. Immediately after injury the anatomical elements of the surfaces of the wound are to be sharply and distinctly distinguished.   But after a few hours they are no longer distinct, while a thin, gelatinous, no longer removable liquid not only covers them, but also infiltrates their superficial layers. In consequence of the hyperæmia produced by the injury itself, and by thrombosis of the vessels, there appears an albuminous exudation for the most part with small hæmorrhages.   The borders of the wound swell, partly from the hyperæmia, exudation, and hæmorrhage, partly from the new-formation of cells beginning after a few hours, and are reddened.   A few days after injury a necrosis of the parts immediately adjacent to the wound appears, as well of those affected by the injury itself as of those which suffer diminished nutrition from their firm inclosure with coagulated fibrin.   The

extent of necrosis in healing by first intention is always very small. The necrosed particles are for the most part absorbed.

DEFINITIVE UNION takes place through new-formation of connective tissue and vessels. The basis substance of the connective tissue of the borders of the wound loses its fibrous structure, becomes homogeneous and gelatinous. According to many, its corpuscles and capillary nuclei divide and become at first round, sometimes spindle-shaped cells, which secrete a new basis substance, and thereby determine union; according to others, this takes place from migrated colorless blood-corpuscles. In place of the closed vessels lying nearest the surface of the wound, there are formed new vessels, which enter into communication with the vessels of the opposite side : upon this the reddened and swollen borders of the wound become pale and the swelling decreases.

GRANULATION-TISSUE is a homogeneous, gelatinous, or only indistinctly fibrous basis substance, with numerous, rounded and spindle-shaped, uninuclear, more rarely multinuclear cells, and with an abundant supply of capillaries, which are partly original, but are for the most part new-formed (INFLAMMATORY NEW-FORMATION, primary cell-tissue, plastic infiltrated, plasmatic tissue, *akestoma, i.e.*, tissue of repair).

The oldest, Hunterian view, whereby union of wound-surfaces takes place by a layer of plastic lymph, is not confirmed by microscopical investigation. WYWODZOFF concludes from experiments, that the red blood-corpuscles and the fibrin of the blood become intercellular substance, the colorless blood-corpuscles become connective tissue and vessels. (?) According to the experiments of THIERSCH, who made incised wounds in the tongues of guinea-pigs and rats and injected them at varying periods after the cuts, no intermediate substance exists at all in the wound, but the appearance of it is due to the blood and albuminous liquid infiltrated into the wound-surfaces. The further changes now take place in part between the vessels where there is an abundant new-formation of cells, in part in the vessels themselves. The latter also and the capillaries, as well as the smaller arteries and veins, suffer an infiltration of their walls with granulation-cells. Between the latter the blood flows out of the interior of the vessel through the finest pores, permeable also to the matter injected, into the intermediate spaces of the granulation-cells (which may likewise be artificially injected), and return by another vessel-wall again into the interior of the vessel. This passage, which results after a few hours, takes place more quickly from capillary to capillary than from arteries to veins. The capillaries, soon after the injury, are metamorphosed, at first at the cut end, by growth of their nuclei, into solid cellular cords with intercellular channels, which are supplied with blood-plasma from the open part of the capillary tube. In the larger vessels this takes place by growth of their endothelium, etc. Most of these provisional intercellular channels disappear, while some dilate and a wall is formed by the cells surrounding them ; the intermediate isolated cells become connective tissue. Finally, the vessels originally present and affected by cell-growth return to their normal state.

How LYMPHATIC VESSELS behave is still unknown ; the original vessels are probably destroyed ; new vessels are formed only after the formation of bloodvessels. See LÖSCH (*Virch. Arch.*, XLIV., p. 385).

γ. The processes in HEALING BY SECOND INTENTION are essentially the same. But a direct cementing of the borders of the wound is wanting. On the other hand, after cessation of the larger hæmorrhage, on the second or third day, there flows from the wound-surface a thin, sero-sanguineous liquid, which in part proceeds as continuous hæmorrhage from small vessels, in part is the product of inflammation of the borders of the wound. This liquid becomes gradually clearer, contains fewer blood-corpuscles, and, from the third to the fifth day, approximates the character of common pus. On the second to the fourth day after injury, the necrotic portions are separated with the liquid of the wound, with the removal of the charpie, etc. These

portions are very small, often larger in tendon, fascia, and bone. They form with the extravasation and exudation for the most part a brownish, greasy, sometimes peculiarly smelling substance. A wound, whose appearance at first resembles that above described, is, on the second to the fourth day, of a dirty red color, has a disagreeable odor, and its proper constituents are no longer to be distinguished: it is "dirty." On the third to the fifth day it is pale red, soft, smooth, or somewhat uneven, but does not yet granulate: it "cleans off." On their surface there is in parts a throwing off of very small necrotic shreds of tissue, in parts suppuration. Only on the fourth or fifth day after injury, with a continuous secretion of pus on the surface of the wound, are there to be seen a large number of small, rounded, firm, wart-like protuberances, so-called GRANULATIONS. The latter increase in size, softness, and number, until finally the whole wound is filled with them. At this time in granulating suppurating wounds there can be distinguished two layers: one superficial, so-called PYOGENIC LAYER, which consists mostly of multi-nuclear pus-corpuscles (incapable of farther tissue-formation) and a mucous basis substance, which is gradually removed and is formed out of the deeper layer, and a deeper, so-called PLASMATIC LAYER, which resembles the granulation-tissue described above. Both layers pass gradually into normal tissue. After granulations and suppuration have existed many days or weeks, the secretion of pus becomes less; the granulations gradually become smaller, less circumscribed, firmer, more anæmic, and become vascular, at first fibrous, then fibrous connective tissue. The vessels and basis substance at first persist, the abundant round cells of the surface pass away, while those of the deeper portions are in part absorbed, in part transformed into connective tissue-corpuscles.

The CICATRIX arising by first, as well as by second intention, is at first very vascular, soft and tender. It gradually becomes paler, more anæmic, firmer and smaller: so-called CONTRACTION OF CICATRICIAL TISSUE. Cicatrization is at first introduced by obliteration of the superficial vessels of the granulations and disappearance of the homogeneous intercellular substance. Thereby fibrous lines are formed, which are surrounded by fibre-cells. The granulations themselves therewith become more diffuse and paler.

Finally, at first, for the most part, on the border, rarely separated from it, in suppurating wounds with cessation of suppuration, there is formed YOUNG EPIDERMIS. It does not proceed from granulation-tissue, but from the surrounding, etc., epithelium.

Granulations are not an imitation or remnant of the papillæ of the skin, but new-formations of a peculiar, young, vascular connective tissue in form of papillæ. In the skin they correspond to the papillæ; in the subcutaneous cellular tissue, however, they lie between the small fat-lobules, in muscles, tendons, etc., between the single fibre-bundles: they correspond with parts of organs, which are especially vascular and capable of a very abundant exudation.

Granulations show at different periods of their existence a somewhat different structure. At first they consist of the homogeneous connective tissue of the wound, and of cells which partly resemble colorless uni-nuclear blood-corpuscles, are partly spindle-shaped, in part they represent intermediate forms. Immediately after, within a few days, numerous capillaries appear in the granulations, spindle-shaped cells exceed the round in number, become longer, their processes filamentous, their nucleus larger. Now the granulations consist of a soft, homogeneous, mucus-containing tissue, which is in part the remains of the old tissue, but especially the product of new-formed, or migrated cells, and of fibre-cells with two or more processes as well as of some pus-corpuscles. The vessels of the granulations are very numerous, form at their points a dense, swollen net-work filled with blood, from which are given off at their base two or more, thicker or thinner capillary

branches, which connect every net-work with the original vessels of the part. The capillaries of granulations like common capillaries, have especial nuclear walls and can be artificially injected. Nerves and lymphatics have never with certainty been observed in granulations. Their surface is at first without epithelium. This construction of granulations, especially their vascular arrangement, explains the continuous exudation of plasma and emigration of blood-corpuscles on their surface. The deep layer of the granulations and the tissue, with which they are connected by their base, is distinguished only by its greater firmness, increased fibrous character, fewer vessels and more abundant fibre-cells.

Granulations are in many cases EXUBERANT and FUNGOUS (*caro luxurians*, "proud flesh"): they then project fungus-like beyond the limit of the neighboring tissues, are usually very soft, for the most part richer in vessels, sometimes poorer in them; the secreted pus is mucous, poor in cells. Fungous granulations show, according to RINDFLEISCH, a more distinct perfect stroma, which is similar to that of the lymph-follicles; sometimes in places, aggregations which consist of mucous tissue. Sometimes there occur therein so-called giant-cells with many processes and numerous nuclei. Granulations are called ERETHISTIC, which are very painful and are mostly exuberant and bleed easily. In a case of so-called irritable granulations RINDFLEISCH found a great abundance of nerve-fibres. Concerning further diseases of granulations consult HEIBERG (*Virch. Arch.*, 1872, LV., p. 257).

In erysipelas of the surrounding structures, in pyæmia, in all severe diseases toward the end of life the granulations become smooth, red, shining, and secrete a thin serous liquid.

A variety of healing by second intention is HEALING WITH THE FORMATION OF SCABS. This healing in a dry way is the rule in animals, so that in experiments very little or no pus is obtained. In man this occurs more rarely (mostly in small, less suppurating wounds), or where it appears or would appear, is prevented by the surgeon. It is found in common incised wounds, wounds from burns, rarely in wounds already granulating. The SCAB or CRUST consists of blood, pus, other wound-secretions, as well as of dirt or of powder, of different kinds, etc., which have been applied to the surface of the wound. The crust remains attached to the wound, until cicatrization appears. The latter is distinguished from common cicatrices formed by healing by second intention, by the absence of cicatricial contraction.

Sometimes cicatrices do not become contracted, but HYPERTROPHIED, so that they represent tumors of varying size. Especially is this the case in small wounds, suppurating for a long time, after the introduction of ear-rings, in cicatrices after burns, especially with powder, burning oil. Their tissue then has a cytogenic structure; and not infrequently contains giant-cells.

CICATRICIAL CONTRACTION, so-called, which regularly occurs in wounds healing by first and especially by second intention, in numerous, especially plastic operations, in wounds near the eyes, mouth, etc., in wounds from burns, etc., deserves especial regard on the part of the practical surgeon. Indeed it is sometimes of service, *e.g.*, for the healing of entropium. Its causes in general reside in the obliteration of new-formed vessels and consecutive atrophy of connective tissue. Under especial unknown condition it appears remarkably great in even small wounds.

Cicatricial formation follows in various individuals in different periods, without the possibility of its cause being suggested. In many men wounds of all kinds heal very quickly, often in tuberculosis and cancer (namely, the extirpation-wounds of epithelial cancers); in others, healthy as well as especially drinkers, cicatrization is usually slow.

The HEALING OF WOUNDS OF TENDONS, MUCOUS MEMBRANES, GLANDS, as well as REPAIR of PARTS OF THE BODY ALMOST or ENTIRELY SEPARATED (tip of the nose, ears, fingers, etc.), goes on in essentially the same manner as healing of wounds of the skin.

The FORMATION OF SO-CALLED CAPSULES about foreign bodies, *e.g.*, grains of shot, bullets, needles, etc., about PARASITES, occurs in the same way in organs of every kind.

The surgically important regeneration of tendons after subcutaneous section was first shown by PIROGOFF, especially by THIERFELDER, then by BONER, ADAMS, and others.

Whether in these cases, granulation-cells, as has been generally assumed until recently, arise from connective-tissue corpuscles, or at the same time from the capillary nuclei, from gland-cells in glandular organs; or whether they are in part migrated colorless blood-corpuscles, has not yet been determined. The gland-cells lying nearest to the wound are wholly destroyed. According to HOLM and STRICKER (*Wien. Sitzgsber.*, March, 1867, p. 493) in traumatic hepatitis, hepatic cells are transformed not only into fatty granular cells, but also into fibres, so that granular cells next become granular fibres. Hepatic cells thus furnish a part of the material of fibrous cicatricial tissue. Another metamorphosis of liver-cells is a transition into so-called granulation-cells.

B. NEW-FORMATION OF VASCULAR CONNECTIVE TISSUE IN THE FORM OF SO-CALLED CONNECTIVE-TISSUE HYPERTROPHY, OR OF CONNECTIVE-TISSUE INDURATION.

CONNECTIVE-TISSUE HYPERTROPHY occurs very often and in almost all organs. It consists sometimes in hypertrophy of the common firm fibrous connective-tissue, sometimes in the formation of soft, gelatinous connective tissue, sometimes in an increase of mucous tissue with subsequent metamorphosis of it into homogeneous or fibrous connective tissue, sometimes finally in a transformation of capillaries, structureless membranes, etc., into a substance like connective tissue. The vessels sometimes take no part therein, they sometimes increase in like manner, sometimes they are in varying number destroyed.

Connective-tissue hypertrophy affects either the whole organ or only parts of organs. Herein it is represented very differently. In general, the organs or parts of organs become larger and for the most part firmer, with varying vascularity. Their function is sometimes left intact, sometimes to a great degree destroyed: the latter especially in consequence of diminished mobility of organs, in consequence of the frequent consecutive destruction of vessels (functional and nutritive) and of the softer, especially glandular textures.

Connective tissue hypertrophy and connective tissue tumors of many organs, especially the skin and mucous membranes, often pass without limits into one another.

The CHANGES of new-formed connective tissue are the same as those of normal connective tissue and of that formed during healing of wounds. CICATRICIAL CONTRACTION is most important with respect to glandular organs (liver) and those surrounded by vascular membranes (brain, etc.): it is followed by diminution of supply of functional or nutritive blood, and through both conditions, diminished nutrition and function of organs. Also worthy of note are œdematous infiltration, hæmorrhage with formation of pigment, inflammation with suppuration, calcification, etc.

The CAUSES of connective tissue hypertrophies are most frequently diminished circulation of blood and lymph, the former from various causes, the latter from increase of endothelium; also often repeated acute and especially chronic inflammations (so-called inflammatory hardening or induration, see p. 271); many poisons (alcohol) are sure causes of drinkers' or granular liver—phosphorus: if both are used in comparatively small doses for a long time. The causes are often unknown.

HELLER (*Arch. f. klin. Med.*, 1872, X., p. 141), in a case of scleroderma with scattered denser points and similar affections of the muscles, heart, intestines, etc., in a woman 56 years old, found an obliteration of the thoracic duct with dilatation of the afferent and smaller lymphatic vessels and inflammatory growth of the endothelium. The author saw a similar condition in elephantiasis.

If rabbits, cats or dogs be fed for many months with minimum doses of phos-

phorus and the dose increased slowly and continuously, so that no acute or subacute intoxication be experienced, the stomach and liver will show a high degree of connective tissue hypertrophy. The gastric mucous membrane becomes twice or three times thicker, indurated, and of a smoky gray or brown diffuse color. In the liver there is developed either a smooth induration, or a lobing of the liver similar to that of syphilitic induration, or true cirrhosis; always with atrophy of the liver-cells, and various stages of connective tissue development, and chronic icterus. In the latter forms there appear venous hyperæmia of the gastric and intestinal mucous membrane, chronic tumor of the spleen, finally ascites and hydro-thorax. (WEGNER, *Virch. Arch.*, 1872, LV., p. 11.)

KUSSMAUL and MAIER (*Arch. f. klin. Med.*, 1872, IX., p. 283) found in a case of chronic lead-poisoning, stronger development of the sub-mucous tissue of the stomach and intestine, growth and sclerotization of the connective tissue septa of many ganglia of the sympathetic nerve, especially of the cœliac and superior cervical.

Increase of connective tissue takes place PHYSIOLOGICALLY in the mucous membrane of the uterus during menstruation, and especially during pregnancy. The mucous membrane thickens already in the second week of pregnancy, especially that of the body of the uterus to from four to six millimetres, is softer, redder and plaited, and finally becomes the decidua vera. The latter contains in a comparatively scanty connective tissue, very abundant cells, especially lines of large, nucleated, spindle-shaped cells. In the later periods of pregnancy, it consists of a structureless substance with more epithelium-like cells and free nuclei. The various stages of growth and disappearance of the decidua are not yet certainly known.

Consult DENMAN, *The Anat. of the Human Gravid Uterus*, 1774.—SIMPSON, *Obstetric Memoirs and Contrib.*, 1855, I., p. 283.—VIRCHOW, *Ges. Abh.*, 1856, p. 735.—HAUSMANN, *Beitr. z. Geburtsh. u. Gynäk.*, 1871, I., 2 H., p. 155.

The pathological connective-tissue hypertrophies most worthy of notice are the following:

HYPERTROPHIES OF THE SKIN are hereditary or acquired, partial or extended over a varying extent, pure or with simultaneous growth of epidermis, papillar and vascular growth, new-formations of fat, growth of hair, pigmentation, etc.; and affect sometimes both layers of the skin, sometimes only or especially the upper and lower, sometimes also the subcutaneous tissue, sometimes at the same time the deeper connective-tissue layers (even the periosteum and bones).

Here belong: PACHYDERMIA or ELEPHANTIASIS ARABUM; *pachydermia nostras* with its sub-varieties (*eleph. lævis s. glabra, el. papillaris s. verrucosa, el. tuberosa s. nodosa—el. alba, fusca* and *nigra—el. cornea—el. mollis* and *dura*—common and ulcerous el.—*el. teleangiectodes—el. cystica*), of the extremities, especially the lower, as well as of the male and female genitals;—true KELOID; so-called scleroma of the skin; the induration in the neighborhood of chronic ulcers; many cases of so-called tumor albus. In part also there belong here ichthyosis and horny growths, warts, and condylomata, many soft warts, molluscum simplex, *nævus mollusciformis*.

The remarkable case of a man covered at birth with innumerable soft warts, which reached the size of a dove's egg, whose skin, tanned and stuffed, is to be found in the collection at Leipzig (TILESIUS, *Von Reinhardt's Disease*, 1793), as well as the case which forms the frontispiece of VIRCHOW's *Geschwülsten* likewise belong under this classification. I know a man fifty years old, who bears a perfect resemblance to the case above described: his affection is hereditary; a son of this man is troubled with the same disease.

KELOID is a formation of the skin similar to a hypertrophic cicatrix, of varying size, 1 to many mm. high and of varying form, often with processes. Its resemblance to cicatrix depends especially upon its whitish, bright surface and on the thinness and firm adhesion of the overlying skin. It occurs for the most part singly, rarely in numbers; most often on the sternum and body. It occurs sometimes after local injuries of the skin, sometimes in or around a cutaneous cicatrix. Histologically, keloid resembles in part cicatricial tissue, in part fibrous sarcoma. In the periphery there are found in the processes of keloid numerous nuclear spindle-shaped cells, which lie like sheaths on the walls of the vessels, especially those of the arteries; the older central parts of keloid, on the contrary, contain much less

of these cells, but especially connective tissue.—Consult ALIBERT, *D. ser. d. mal. de la peau*, 1814, p. 113.—*Mem. de la soc. méd. d'émul.*, 1817, p. 744.—FOLLIN, *Gaz. d. hôp.*, 1849, No. 75.—LANGHANS, *Virch. Arch.*, XL., p. 332.—KOHN, *Wien. med. Wschr.*, 1871, Nos. 24-26.

On RHINOSCLEROMA consult HEBRA, *Wien. med. Wschr.*, 1870, No. 1.—GEBER, *Arch. f. Dermat. u. Syph.*, 1872, IV., p. 493.

HYPERTROPHIES OF MUCOUS MEMBRANES affect a greater or less extent of surface, the papillary layer only, or the entire tissue of the membrane (or simultaneously the sub-mucous tissue, intermuscular connective tissue, muscular and serous layers). With these there not infrequently occur hæmorrhages, hypertrophy or atrophy of glands, etc.

Here are included the simple thickenings of mucous membranes, especially after chronic catarrhs, polypous and plaited hypertrophy of mucous membranes. (*e.g.*, on the internal surface of many bronchiectasiæ), and partly polypi of mucous membranes. The surface of these mucous membranes is (mostly in consequence of dilatation of the glands) often covered with an abundant, transparent or pasty mucus. These hypertrophies, in one form or another, affect especially the mucous membrane of the nose, bronchi, stomach, large intestine, uterus, the decidua vera.

HYPERTROPHIES OF FIBROUS MEMBRANES are found in periosteum and perichondrium as primary or as consecutive processes; likewise in muscle-fibres; often in the dura mater (so-called pachymeningitis chronica), in the tunica albuginea of the testicles and ovaries, especially in old people, in the fibrous coat of the spleen, kidneys, in the neurilemma, in the sclerotic and cornea. Hypertrophies of tendons and ligaments, as well as of the connective-tissue portion of fibrous cartilage occur mostly in chronic inflammations and with like affections of the bordering parts, especially the bones.

HYPERTROPHIES OF VASCULAR MEMBRANES, of the pia mater and of the choroid plexus, of the iris, etc., often occur as general or partial clouding, thickening, etc.

KUSSMAUL and MAIER (*Arch. f. klin. Med.*, 1866, I., p. 484) found in a clinically remarkable case (quickly arising general muscular paralysis with loss of electric contractility, severe pains, small subcutaneous tumors, etc.) peculiar thickening of numberless fine arterial branches, dependent upon new-formation of cells, nuclei and connective tissue in the adventitia and upon nuclei in the muscle-cells of the media: so-called PERI-ARTERITIS NODOSA. Thereby the vessels are sometimes dilated as aneurisms, sometimes contracted.

HYPERTROPHIES OF HOMOGENEOUS CONNECTIVE-TISSUE MEMBRANES, as of the envelopes of the Malpighian bodies of the spleen, solitary and Peyer's follicles, etc., also of the so-called membranæ propriæ of most racemose and saccular glands, testes, Graafian follicles, Malpighian bodies of the kidneys, urinary tubuli, liver, etc., occur frequently, rarely alone, for the most part with various chronic changes of glandular elements, surrounding connective tissue and capillaries.

HYPERTROPHIES OF AREOLAR CONNECTIVE TISSUE likewise affect the tissue in all localities: FAT-TISSUE under the skin, that of the bones, in the abdominal cavity, etc., rarely alone, mostly at the same time with the overlying parts (*e.g.*, skin, peritoneum), often in the neighborhood of chronic ulcers, fistulæ, carious bones, etc.

SUB-SEROUS, SUB-MUCOUS, INTER-MUSCULAR AND INTER-ACINOUS CONNECTIVE TISSUE, loose connective tissue in the vicinity of the large intestines, vessels and nerves, interstitial nerve-tissue, etc., show hypertrophies of

varying extent and degree, which rarely occur alone, but for the most part with chronic inflammatory processes in the surrounding tissues.

Through hypertrophy of sub-mucous tissue there arises a condition of the gastric mucous membrane similar to the mammilated state : so-called granular degeneration of FREUND. (*Abh. d. schles. Ges. f. vat. Cultur.*, 1862).

In GLANDULAR ORGANS (mammæ, ovaries, liver, pancreas) there arise many so-called hypertrophies, indurations, CIRRHOSES, etc., which are of various forms, according to whether the whole connective tissue or only that of some parts, *e.g.*, in the mamma, in lymph-glands that of the hilus, is hypertrophic. At the same time the gland-cells are for the most part destroyed.

In the mamma the affections of this class are called hypertrophies or innocent induration, or diffuse fibromata, also hard elephantiasis, cirrhosis, etc., if they affect the whole mamma ; fibroid, fibroma tuberosum s. lobulare, if they are partial. The changes in the liver, spleen and kidneys in consequence of chronic diseases of the heart likewise belong here ; they are often combined with degenerations of glandular elements. In connective-tissue indurations of lung-tissue, the connective tissue around the bronchi and vessels, as well as the interlobular connective tissue, is sometimes thickened to a great degree; from these connective-tissue fibres are seen to radiate into the alveolar tissue of the lungs themselves, so that the alveoli are, as it were, pierced by connective tissue. Cirrhosis proper of the liver and granular kidneys are of the greatest importance.

C. NEW-FORMATION OF VASCULAR CONNECTIVE TISSUE IN THE FORM OF CONNECTIVE-TISSUE TUMOR.

New-formation of connective tissue and vessels occurs in ALMOST EVERY TUMOR. Both tissues form the capsule, or the pedicle, or the sheath (so-called stroma) of the tumor. Or they together form the greatest part of it. Only the latter new-formations here come under consideration. On their modes of origin, see p. 373.

a. TUMOR OF FIXED OR FORMED CONNECTIVE TISSUE, SO-CALLED FIBROMA OR FIBROID.

(FIBROMA DENSUM S. COMPACTUM, TRUE CONNECTIVE TISSUE OR FIBROUS TUMOR, fibrous tumor, desmoid, inoma ; formerly called also chondroid, scirrhus, steatoma.)

SOLID FIBROMA consists mostly of distinct connective-tissue fibres, which are arranged in every possible direction, and on this account are with difficulty isolated, rarely of indistinct fibrous or wavy connective tissue : besides, of connective tissue corpuscles in varying abundance, of comparatively numerous vessels, and commonly also of elastic fibres.

Fibromata are for the most part sharply circumscribed, rarely diffuse : in the latter case, they pass into connective-tissue hypertrophies. Their size varies from that of the smallest circumference to that of the uterus far advanced in pregnancy and more. Their form is round, rounded, or oval, etc. ; their periphery uniform, knobby, or lobed. They are solid in section ; section is accompanied by a creaking noise. The cut-surface is even, shining, for the most part whitish, rarely gray, grayish-red, yellowish-red, commonly also without visible vessels. It is dry, or shows only a very small quantity of serous, sometimes slightly mucous liquid. It is concentrically laminated, sometimes uniformly, sometimes about one or more central points, sometimes it is composed of irregularly intersecting fibre-bundles,

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sometimes it consists of variously formed parts separated by soft connective tissue. It offers mostly a distinct fibrous character; it is rarely entirely homogeneous.

BILLROTH (*Arch. f. klin. Chir.*, IV., p. 545) refers the peculiar architecture of fibromata to the fact that they arise from nerve-sheaths and the adventitia of the smaller arteries; the nerves disappear, the arteries remain. By this it is explicable why in the uterus, nerves and vessels of which undergo a considerable change in dimensions during menstruation and pregnancy, and in whose sheaths there is a constant morphological movement, fibromata so often arise; why they are so rich in arteries, which bleed profusely after every injury, because they cannot retract; why many nerve-tumors pain only for a length of time or not at all, whilst the nerve-fibres are gradually destroyed.

Fibromata OCCUR on the trunk and extremities, proceeding from the skin (as elephantiasis tuberosa, etc.), from the subcutaneous and intermuscular connective tissue, from fascia, periosteum, bones, and bone-marrow; in the uterus and its vicinity, in subserous tissues chiefly, in submucous tissue, especially of the nose and throat, more rarely in that of the larynx, stomach, and intestines; in nerves (as common neuroma, and as so-called subcutaneous, painful tumor, or so-called irritable tumor); in glandular organs, especially the mamma, kidneys (*nephritis interstitialis tuberosa*), etc.; very rarely in the liver, heart, etc.

Fibromata occur in the skin almost always SINGLY. They rarely return after extirpation. Only in some cases are fibromata METASTATIC, especially in the lungs and serous membranes. Organs and tissues, which are the seat of fibromata, as well as the whole organism, suffer almost always only from the size of the tumor.

Fibromata for the most part GROW very slowly.

The METAMORPHOSES of fibromata affect one or many points, rarely the whole tumor. They are: HÆMORRHAGES with consecutive pigmentation, perhaps also cyst-formation; CALCIFICATION, not infrequently in some parts of the centre, more rarely in the periphery, it makes the consistence of the tumor sometimes only crumbling or chalky, sometimes of stony hardness; OSSIFICATION, rarely, for the most part only at points; FATTY METAMORPHOSIS, whereby some parts of the tumor are yellowish and soft, sometimes cavernous; INFLAMMATION, sometimes with formation of abscess, more often with consequent ichor; sometimes with spontaneous elimination. Absorption of fibromata is very questionable.

The COMBINATIONS of fibromata with other forms of tumor are comparatively frequent. They are either present from the beginning: so-called combination proper; or they are formed in developed fibroma: so-called degeneration. Especially noteworthy are: here and there new-formation of MUCOUS TISSUE, fibroma myxomatosum (not to be confounded with œdema of the same.); LIPOMATOUS metamorphosis, fibroma lipomatodes, rare; new-formation of ORGANIC MUSCLE-FIBRES, the earlier so-called fibroid (see Myoma); SARCOMATOUS degeneration, which in its lightest degrees not infrequently occurs in the form of striæ, which consist of spindle-shaped cells lying close together, and sometimes affects the original, sometimes the recurrent (after extirpation) tumor (fibroma sarcomatosum); CAVERNOUS DEGENERATION, whereby fibromata here and there or throughout are like the pregnant uterus; combination with CYSTS.

b. TUMOR OF LOOSE, OR AREOLAR CONNECTIVE TISSUE.

So-called FIBROMA AREOLARE S. LAXUM; cellular tissue fibrous tumor (J. MÜL-

LER), connective tissue tumor (J. Vogel), albuminous fibroid (Schuh), fibro-cellular tumor (Paget).

Areolar fibroma consists of bundles of vascular, fibrous, or homogeneous connective tissue, which presents spaces of varying number, size, and form, filled with serous or mucous liquid. It shows manifold transitions into solid fibroma and connective tissue hypertrophy.

In many areolar fibromata there are found only spaces which correspond to dilated lymphatic vessels and to transitions of these into the normal vessels.

Waldeyer (*Arch. f. Gynäk.*, 1871, II., p. 440) describes a diffuse fibroma of the ovary, of peculiar construction: its cut surface bears a similarity to spongy bone with narrow meshes.

Areolar fibromata are of very varying size, which is not infrequently considerable, and of a regularly rounded, uniform, or lobed form. Their surface is for the most part light-yellow and soft. The cut-surface shows a color and lobing which correspond to those of the surface. The lobes are mostly separate from one another, here and there connected together. The surface of section sometimes resembles œdematous connective tissue and gives out an abundant quantity of liquid, whereby the tumor collapses, becomes firmer, and like common fibromata; sometimes it contains numerous cyst-like spaces.

Areolar fibromata occur in circumscribed or diffuse form. The former are found in the skin and subcutaneous connective tissue, especially of the scrotum, labia majora, around the vagina, in intermuscular connective tissue, periosteum, in the bones of the extremities, in the uterus, mammæ, etc. The latter occur oftenest in the skin of various parts, as so-called soft warts, molluscum lipomatodes, cutis pendula, fibroma molluscum, and as leontiasis; also as elephantiasis of the scrotum, prepuce, labia, clitoris, of the extremities, nose, ears; as well as, finally, in the submucous connective tissue of the pharynx, nose, larynx, uterus, etc., in form of so-called polypi.

Various metamorphoses (fatty, chalky, pigmentary) are very often found in these tumors; also abscesses in various stages of development; or slight admixture of fatty, cartilaginous, sarcomatous tissues, etc., whereby the character of the surface of section may become in the highest degree mixed. If the tissue last-mentioned occurs in greater quantity, the tumors become lipomata, enchondromata, sarcomata, etc.

c. Mucous tissue tumor, or mucous tumor, myxoma.

Tumor mucosus, collonema, gelatiniform or colloid sarcoma.

J. Müller, *Arch. f. Anat. Phys.*, etc., 1836, CCXIX.—Virchow, *Arch.*, 1857, XI., p. 286; *Die Geschwülste*, I., p. 396.

Myxoma occurs pure or mixed with other tissues.

Pure myxoma consists, besides, of a scanty connective tissue poor in vessels (but which may also be wanting), only of mucous tissue, *i.e.*, of a mucous basis substance with stellate or spindle-shaped cells anastomosing with one another, or (in young tumors) with small round cells like mucous corpuscles.

Pure myxoma forms soft, frequently fluctuating, translucent masses, for the most part poor in blood, which on section usually shows various septa of connective tissue, and a soft or firm gelatinous consistency, and by pressure there escapes a colorless, or pinkish and viscid mass. The tissue is,

according to its cell-contents, translucent, clear: MYX. HYALINUM s. gela-
tinosum,—or cloudy, whitish, even medullary: MYX. MEDULLARE.

MIXED FORMS OF MYXOMA are: MYX. FIBROSUM, which contains a more
abundant connective tissue, or also elastic tissue; MXY. TELEANGIECTODES,
with abundant vessels; MYX. LIPOMATODES, which by its fat-cells appears
yellow, uniformly or in spots; MYX. CARTILAGINEUM, which contains car-
tilage-cells.

Myxomata are more often HYPERPLASIÆ, less often heteroplastic forma-
tions. To the former belongs especially myxoma of the placenta, the so-
called vesicular mole, which consists in a hypertrophy of the mucous tissue
of the tufts of the chorion, for the most part in the whole circumference of
the membranes of the ovum. The tufts become converted into pedicled,
vesicular forms, which vary in size to that of a cherry and larger, and which
not infrequently have smaller tumors attached to them; the whole mass
may reach the size of a man's head. Either there is no longer any trace of
the fœtus visible; or in the interior of the whole mole there are yet to be
found the remains of it, as well as of the amnion, umbilical vesicle and cord.
Sometimes the tufts only of the chorion are degenerated into myxomata;
the placenta otherwise normal, the fœtus develops correspondingly with
the time of pregnancy.

With respect to many myxomata it is not to be distinguished, whether
they are of hyperplastic or heteroplastic nature. To these belong those in
the subcutaneous and intermuscular connective tissue, in fasciæ—especially
of the thigh, back, hand, cheeks, corners of the mouth, labia; also those in
peripheric nerves; perhaps also in bones, especially in their medulla, es-
pecially of the maxilla and tibia.

Myxomata are heteroplastic in the interior and in the vicinity of glandu-
lar organs (salivary glands, mammary glands, testicles, thyroid gland); less
often those in the brain and its meninges, those in mucous membranes
(urinary bladder), etc. Many myxomata which seem heteroplastic, are per-
haps hyperplasiæ, while remains of mucous tissue from the fœtal period
persist, without, as normally happens, becoming transformed into fatty
tissue.

Myxomata mostly have the form of tumor; in rare cases they are diffuse
(many so-called hypertrophies of the mammæ). The tumors are mostly
round and uniform, rarely lobed; they are for the most part small. They
are mostly single; multiple sometimes only in the nerves. They rarely
return after extirpation. They seldom form metastases.

Myxoma of the placenta (so-called vesicular mole), long known clinically (BOIVIN,
Nour. rech. sur l'orig. de la môle résiculaire, 1827), has been more accurately investi-
gated histologically during the last ten years. Consult especially H. MÜLLER, *Ueb.
d. Bau d. Molen*, 1847. MECKEL and GIERSE, *Verh. d. Berl. geburtsh. Ges.*, 1847,
II, p. 126. BLOCH, *Die Blasenmole*, 1859. The vesicular mole occurs more fre-
quently during the later years of life (40th–50th year). Its other causes are
unknown. Aside from the destruction of the fœtus, it becomes important through
the hæmorrhages during the expulsion, which sometimes are very profuse, through
puerperal inflammations, etc.

JAROTZKY and WALDEYER (*Virch. Arch.*, 1868, XLIV., p. 88) describe an intra-
parietal and intravascular further development of chorion-tufts in myxomatous de-
generation, and suppose, that by a longer intra-uterine existence of the mole (about
the third month) a growth of the chorion-tufts into the blood-spaces of the uterine
substance must take place.—VOLKMANN (*Ib.*, XLI., p. 528) earlier described a case
of interstitial destructive mole-formation.

WALDEYER (*Ib.*, XLIV., p. 83) saw an arborescent myxoma of the SEMINAL DUCT,
which was independently developed in the veins, the lumen of which was filled, and
which formed a part of a myxo-chondro-sarcoma kystomatosum of the testicle.

A diffuse new-formation of mucous tissue, which occupied the greatest part of the gray substance of the CEREBELLUM, was found by BILLROTH (*Arch. d. Heilk.*, III., p. 47). All small vessels and capillaries were surrounded by a thick adventitia, which consisted of mucous tissue.

W. MÜLLER (*Beob. d. path. Inst. zu Jena*, 1871, p. 481) describes the myxomatous adenoma of the thyroid gland and determines its relation to the common gelatinous goitre (adenoma gelatinosum—see p. 330) and to colloid cancer. Myxomatous adenoma forms in the thyroid gland either sharply circumscribed and capsule-like deposits, or uniform infiltratious not sharply defined. The starting-point of myxoma-formation is, according to M., the adventitia of the smaller arteries.

WEICHSELBAUM (*Virch. Arch.*, 1872, LIV., p. 166) describes a great myxoma with SECONDARY tumors of the lungs: in both localities were found also scattered isolated formatious of cartilage and bone.

On other modes of occurrence of mucous tissue, see Compound new-formations.

D. VASCULAR TUMOR, OR ANGIOMA.

(Tumor vasculosus.)

Consult the surgical works, etc., of J. BELL, SCHUH, CRUVEILHIER, ROKITANSKY, and others, as well as VIRCHOW, *Geschw.*, III., 1 H., p. 306.

VASCULAR TUMORS are characterized by this, that they, besides consisting of connective tissue and other common atrophic tissues of the place of origin, consist essentially of new-formed and of original, and for the most part of dilated vessels. The vessels contain BLOOD, which flows more slowly and under higher pressure than in other vessels.

The vessels of angioma are sometimes not distinguished from normal vessels by anything but their great number, sometimes they are dilated to various extents and thinned. There are no other known peculiarities in the structure of the vessels.

Most vascular tumors, like their physiological types, possess the property of ERECTABILITY, *i.e.*, under certain for the most part unknown conditions, also under the influence of heat or by contact, etc., they become larger and harder, of a darker color and higher temperature, and also, in part, pulsating. Angiomata are more frequently found single, rarely in small numbers, most rarely in great numbers. They grow sometimes quickly or slowly, until death, or until they have been cured; sometimes they at length cease to grow; sometimes, finally, they retrograde spontaneously (without demonstrable processes, or by way of thrombosis, inflammation, and ulceration). They act by displacement of normal tissues injuriously in this, that they may give rise in the skin and mucous membranes to erosions and ulcerations, and thereby, not infrequently periodically, to hæmorrhages of dangerous magnitude. Sometimes they are painful. They very rarely return after extirpation.

The mode of development of vascular tumors is still unknown. A portion of their vessels are original vessels greatly dilated. With respect to the remainder of the vessels, they probably arise in one of the ways described above (p. 375) as narrow vessels, which afterwards dilate. Their enlargement takes place probably through granulation-tissue. Many are formed by filling of the net-work of connective tissue corpuscles with blood (NEUMANN, *Virch. Arch*, XXI., p. 280). FLEISCHL (*Oestr. Jahrb.*, 1872, III., p. 229) agrees with ROKITANSKY in regarding the development and structure of cavernous tumors as analogous to that of the structure of cancer. The so-called capsule of angioma is a secondary formation.

The CAUSES of angioma are for the most part unknown. In some cases they are preceded by wounds. In others there is probably at first paralysis of the vasomotor nerves. (The author, *Arch. d. Heilk.*, XI., p. 305.)

Vascular tumors occur chiefly in three different forms.   Besides, there is a lymphatic vessel tumor.

a. TUMOR OF CAPILLARY VESSELS, OR TELEANGIECTASIA PROPER.

(Angioma capillare, erectile tumor, nævus vasculosus.)

It is almost always present at birth, or arises during the first days or weeks of life, rarely in the later years of life, but in the former case increases after birth most quickly in volume. It occurs oftenest in the skin, especially of the head, neck, and extremities, where they are sometimes located in the papillary layer (so-called burnt-mark, mole), sometimes in the entire corium and in the fat-tissue; it is comparatively rare in mucous membranes (especially of the lips); still more rare in muscles, bones, especially in spongy bone-substance, in the tongue, in the choroid plexus, and in the brain.

These tumors are in size from that of a millet-seed to that of the surface of the hand, or occupy a great part of the face or of one extremity, are more rarely circumscribed, mostly diffuse, flat, rarely tumorous, uniform or (especially in fat-tissue) lobed, mostly bluish-red, rarely bright or dark red, soft, and on section appear uniformly red or present some firmer, pale points, and quickly collapse.

The MICROSCOPE shows as the chief constituent tortuous, even cork-screw-shaped capillary vessels in the most varying arrangement, uniformly wide, or varicose or aneurismal, with normal or remarkably thick walls, passing into arterial or venous structure, often strongly contracted, even wholly empty, and on this account recognized with greater difficulty, besides filled with normal blood and rarely with fatty detritus; also small arteries and veins, which are not infrequently similarly thickened. The vessels are in many cases chiefly dilated veins : CAPILLARY VARIX, TELEANGIECTASIS VENOSA s. angioma varicosum. Besides, angioma contains connective tissue, wavy or striped, with scanty nuclei, of uniformly slight or in places of greater strength. In the skin there is frequently found besides, fat-tissue (so-called teleangiectasia lipomatodes), sweat- and sebaceous glands, hairs with their follicles and not infrequently with thickened smooth muscles. Etc.

The so-called glomerular tumor, tumor glomerulosus (BILLROTH), is probably only a very vascular villous cancer.

b. CAVERNOUS, OR VENOUS TUMOR.

(Angioma venosum s. cavernosum.)

It exists rarely at birth, but is for the most part ACQUIRED, in young and old individuals, and proceeds probably in many cases from teleangiectasia. It occurs most frequently in the liver, especially in its periphery, less often in the skin of all parts of the body, especially of the head (region of the ear, lips, eyes, especially in the region of the fœtal commissure : so-called fissural angioma), not infrequently also simultaneously in the bordering mucous membrane; in the subcutaneous cellular tissue, especially in the cheeks and orbits, also the extremities; most rarely in the muscles (also of the tongue), mostly at the same time with the surrounding tissues, in bones, the spleen, kidneys, cerebral meninges, brain, etc.

Cavernous tumors are mostly round, spherical, of varying size, in the liver from the size of a bean to that of a walnut. They are sometimes circumscribed as if encapsuled, sometimes diffuse (*ang. cav. circumscriptum s.*

incapsulatum and *diffusum*) : the former are for the most part smaller and rounder ; the latter may become much larger and appear more flat than tumors. It has the greatest similarity with the cavernous tissue of the penis and clitoris, with the erectile tissue in the mucous membrane of the turbinated bones, with the stroma of the hilus of the ovary, partly also with the tissue of the placenta. After section, the blood is mostly evacuated, the tumor thereafter becomes much smaller and is represented by a grayish-red or gray, loose mass, which here and there sometimes contains older and fresh fibrinous coagula, and phleboliths.

The MICROSCOPE shows a more or less abundant, sometimes throughout tender, sometimes in places denser, sometimes throughout a denser net-work of firm or wavy connective tissue or organic muscle-fibres, the spaces of which contain blood, and thus in many ways they communicate with one another, so that no single vessel can be pursued. The spaces are sometimes provided with endothelium, sometimes not. The remaining elements of the original tissue (liver-cells, etc.) are in places atrophic or have altogether disappeared. The condition of the vessels in cavernous tumors is the same as that in the physiological types referred to : arteries, mostly very small and after extirpation difficult to find, conduct the blood into the cavernous spaces, from which it again flows into the large veins.

Cavernous tumors of the liver, which are most frequently observed, communicate not with one large vessel, but with all the small vessels belonging to the degenerated part (vena portæ as well as the hepatic artery).

In the subcutaneous connective tissue new-formations sometimes occur similar to the cavernous tumors of the liver, but which are sharply circumscribed and are connected at one point with a larger vein (CRUVEILHIER, l. c. ESMARCH, *Virch. Arch.*, VI., p. 34).

ARNDT (*Virch. Arch.*, LI., p. 506) distinguishes three forms of ampullar ectasia of vessels : 1, one, in which the whole capillary wall, the capillary tube and the adventitia are at the same time bulged out and blood flows into the dilatation— COMPLETE AMPULLARY ECTASIA OF THE VESSELS ; 2, one, in which only the adventitia is distended and in the distended part are found only lymph and lymph-corpuscles ; 3, one, which is intermediate between the two former, while both tunics to a certain extent project independently, but are unequally dilated and so project into one another, that the vesicles thus formed contain lymph and blood beside one another, although separated. Both of the last forms are termed by A. INCOMPLETE AMPULLAR ECTASIA OF THE VESSELS, the former ADVENTITIAL ECTASIA.

ANGIOMA VENOSUM in the narrower sense passes in many ways into venous teleangiectasia and is oftenest found in the hæmorrhoidal plexus as external or internal or mixed (sub-cutaneous, or sub-mucous, or half sub-cutaneous, half sub-mucous) hæmorrhoidal tumors, less often in other parts (urinary bladder, etc.).

c. ARTERIAL VASCULAR TUMOR

occurs as ANEURYSMA ANASTOMOTICUM, *tumor vasculosus arterialis, i.e.*, a dilatation and elongation, in parts probably also new-formation of the smallest arterial branches of a definite region, especially of the branches of the temporal and occipital arteries ; and as

ANEURYSMA CIRSOIDEUM s. varicosum s. racemosum, VARIX ARTERIALIS, *i.e.*, dilatation and elongation of both large and small arterial trunks and their branches. It occurs in the same parts. In both cases there are found transitions into teleangiectasia.

d. LYMPHATIC ANGIOMA

consists in a dilatation of the lymphatic vessels analogous to aneurysma cirsoideum. Until now it has been rarely seen, mostly only in combination with elephantiasis, etc., in the skin, lips, conjunctiva, tongue, but occurs more frequently with chronic inflammations (of the skin, serous membranes, dura mater cerebri).

The liquid flowing out of a cavernous lymph-tumor during life was yellowish, clear, of alkaline reaction and soon stiffened into a translucent pale jelly. It contained in 1000 parts 978 water. 8.1 ash, 1.0 fibrin, 1.2 globulin, 5.5 serum-albumen, 5.5 casein, 2.2 chloride of sodium, 1.0 sulphuric acid, 0.2 phosphoric acid and 0.2 lime. (GJORGJEWIC, *Arch. f. kl. Chir.*, 1870. XII., p. 641.)

As LYMPHANGIOMATA OF THE KIDNEYS, HESCHL (*Wien. med. Wochenschr.*, 1866, No. 31) describes sharply defined tumors, from a very small size to that of an apple, which have a lobed surface and very loose consistence, are reddish yellow on section, present free yellowish fatty substance, after the removal of which there remains a finely-filamentous stroma, rich in vessels. The microscope shows sacs arranged parallel with the bloodvessels, which partly anastomose and are filled with molecular fat and granules; the urinary tubuli are compressed. H. regards the tumors as not merely lymphatic ectasiæ, but as in part independent formations.

Consult also KLEBS (*Hdb. d. path. Anat.*, p. 471).

KÖSTER (*Würzb. Verh.*, 1872, III.) showed that a tumor appearing as *hygroma cysticum colli congenitum* was a lymphangiectasia. ARNSTEIN (*Virch. Arch.*, 1872, LIV., p. 319) found in a case of macro-glossia no new-formation of muscle, but the structure of "lymphadenoma cavernosum."

BIESIADECKI (*Unters.*, 1872, p. 11) describes a case of numerous tumors of the skin, which consisted of dilated lymphatic vessels filled with colloid substance.

Many cases of so-called cylindroma probably belong to the class of vascular tumors. HIRSCHFELD (*Arch. d. Heilk.*, 1871, XII., p. 167) proposes for it the name of *angioma mucosum proliferum.*

Concerning so-called plexiform tumors *vide infra.*

E. NEW-FORMATION OF VASCULAR CONNECTIVE TISSUE IN FORM OF PAPILLÆ WITH EPITHELIAL COVERING. SO-CALLED PAPILLARY, OR VILLOUS TUMOR. PAPILLOMA.

ECKER, *Arch. f. phys. Heilk.*, 1844, p. 380.—ROKITANSKY, *Lehrb. d. path. Anat.*, 1855, I., p. 170.—BILLROTH, *Virch. Arch.*, 1859, XVII., p. 357.—VIRCHOW, *Verh. d. Berl. Ges. f. Gebrtsh.*, IV.; *Würzb. Verh.*, I.; *Die krkh. Geschw.*, I., p. 334.

PAPILLARY OR VILLOUS TUMORS, analogous to the vascular papillæ of the skin, villi of the intestines, etc., consist of a for the most part vascular body of connective tissue, rarely of mucous tissue, and of a layer of epithelium.

The CONNECTIVE TISSUE BODY is single or in the most varying manner branched; it is, compared with the whole tumor, thin or thick. The VESSELS of the tumor consist of a single capillary loop or of a larger afferent and efferent vessel with intervening capillary net-work; the tumors are rarely entirely without vessels. The EPITHELIAL LAYER corresponds on the whole with that of the portion of skin or mucous membra from which the papillary tumor arises: it consists sometimes of pavement epithelium of varying thickness (on the skin), sometimes of cylindrical epithelium in one or many layers, or of a kind of transition epithelium (on mucous membranes, etc.).

Papillary tumors occur chiefly on the surface of the skin and of various mucous membranes provided with papillæ or villi; indeed they are found in mucous membranes without villi (stomach, urinary bladder) and in new-formations.

The origin of papillomata varies. In normal parts containing papillæ, they proceed mostly from a simple hypertrophy of all or single parts of the papillæ. In parts without papillæ, there is at first a growth of the connective tissue and vessels; sometimes the vessels later grow into the at first homogeneous basis substance, analogous to the formation of villi on the upper surface of the chorion. The epithelium covering the papillomata is always increased on the tumor: therein it sometimes shows the same conditions as in the normal skin or mucous membrane, sometimes there is a comparatively greater quantity of it. It originates doubtless from the pre-existing epithelium of the part affected.

AUSPITZ (*Arch. f. Dermat. u. Syph.*, 1870, II., p. 25) assumes the contrary mode of formation of papillomata. From many observations on the development of normal skin he concludes, that in the origin of the papillary layer, as in that of the glands and hair-follicles, the epidermis plays an active rôle, that the papillary structure is caused by the active growth of processes inward from the epidermis into the connective-tissue stroma : the papillary boundary of the cutis is formed by the pushing forward by the epidermis of top-like processes into the skin. According to A., papillomata (warts, condylomata, etc.) also arise by an active process in the rete, in consequence of which there results a growing inward of the hypertrophic Malpighian layer into the likewise more or less hypertrophied stroma. The papillæ of the cutis have therein only a passive function; their elongation as well as their dendritic form is dependent upon the hypertrophy of the epidermis, while the elevation of the skin as a whole occurs from the hypertrophy of both, epidermis as well as stroma.

The CAUSES of papillary tumors are in most localities irritants of every kind; in mucous membranes they arise sometimes in consequence of chronic inflammations. Sometimes the causes are unknown.

I saw in a girl, 22 years old, suffering from chronic pulmonary tuberculosis, about 200 true warts, of the size of a pea, appear chiefly on the throat, neck and upper part of the breast; the face and hands were free. After a year there was an eczema-like eruption on the anterior surface of both legs, formations, close together and like warts of the size of a lentil, which remained little changed for 20 years.

The consequences of papillomata vary with their locality : pressure upon the subjacent skin, narrowing of the canal inclosed by the affected mucous membrane, ulceration, hæmorrhages.

Papillary tumors are commonly divided into hard and soft.

HARD PAPILLARY TUMORS consist of a thick, in proportion to the epithelium, single or branched connective-tissue body with comparatively few vessels; or of a thin short connective-tissue body with abundant epithelium forming a horn-like mass. They occur chiefly on the skin, rarely on mucous membranes with laminated pavement epithelium. To this class belong common warts, horns, ulcerating warts, condylomata of the skin, as well as the rare hard papillomata of mucous membranes.

WARTS OF THE SKIN, COMMON WARTS, consist of a comparatively thin, moderately vascular, connective-tissue body arising probably from one or many vascular papillæ, which are surrounded by a very thick layer of epidermis. The warts are hemispherical or consist of single papillæ, according as the latter are or are not surrounded by a common horny layer. Their most frequent seat is the hands.

In warts are included also most CUTANEOUS HORNS, *i.e.*, all those, which at their base contain vascular papillæ.

The so-called MOIST OR ULCERATING WARTS, which occur most often on the lips, and because of their character as well as because of their seat are confounded with epithelial cancer, have a structure like that of common warts, but mostly with a larger area (sometimes a square inch and more). They assume their peculiarities

either at once after their formation, or after having existed for years as common
warts. At first the tumor is better supplied with blood, its surface moistens, the
epidermal cells are thrown off, the papillæ become more distinct, then ulcerate and
are destroyed. At the same time degeneration progresses in the periphery always
beyond the limits of the skin, while the centre continuously secretes an offensive
. purulent liquid, which flows off or forms crusts. Cicatrization rarely begins from
the centre.

COMMON OR POINTED CONDYLOMATA, MOIST WARTS, *cond. acuminatum*, consist
of a more or less regularly branched body of fibrous or homogeneous connective tissue
with a tortuous and tolerably wide capillary vessel in every branch, and of a thin,
easily removable epidermis. The remaining varieties of condylomata are dependent
upon their size, upon the degree of moisture of their surface, and especially upon
their seat on a free portion of skin or near a mucous membrane, or on such, or be-
tween folds of the skin, etc. The seat of condylomata is chiefly the vicinity of the
male and female genitals (neck of the glans, fore-skin, labia minora, inner surface
of the labia majora) and of the anus. According to KRANZ (*D. Arch. f. klin. Med.*,
II., p. 79), papillomata are induced as well by the secretion of moist papillomata
(fresh condylomata), as also by small portions of them introduced under the prepuce
or inoculated into the skin of healthy persons, which papillomata may in two to
three weeks become as long as 1 mm.

To this class belong also the similar, but flat sessile tumors of the skin which are
congenital or acquired : *porrus, verruca sessilis*.

The transition of luxuriant granulations into papillomata forms the fungus-like
papillary tumors (KÖBNER), *framboisia non syphilitica s. dermatitis papillomatosa*
(KOHN).

HARD PAPILLARY TUMORS OF MUCOUS MEMBRANES show manifold transitions
into soft papillomata. Their structure shows nothing worthy of note : their dense
granular appearance is dependent chiefly upon the abundant pavement epithelium
surrounding their moderately vascular and moderately developed connective-tissue
body. They are found in the oral cavity, on the uvula, in the œsophagus, in the
nose, on the vocal cords, in the male and female urethra, in the vagina, on the
cervix uteri, etc., and also on mucous membranes provided with cylindrical epithe-
lium, as the gall-bladder and ducts, milk-ducts—thus in parts, which in the normal
state contain papillæ, as well as in those which normally have no papillæ.

SOFT PAPILLARY TUMORS, VILLOUS TUMORS

consist of tender, single or branched connective-tissue bodies, which
contain very numerous and for the most part wide capillaries, and are
covered by a single or multiple, easily separable layer of pavement or
cylindrical epithelium. They appear sometimes as true villous tumors,
sometimes as spherical or lobed or polypous, soft masses rich in blood,
whose villous character appears only after separation of the epithelial layer
uniting all the extremities of all the villi. Their seat is mostly the other-
wise normal (only penetrated by dilated vessels) mucous membrane. Villous
tumors occur in the urinary bladder, in the vagina, especially in the
vaginal portion (so-called cauliflower growths), in the stomach and intes-
tines, especially the colon, rarely on the internal surface of the dura mater
and on the pia mater and arachnoid. They give rise, according to locality,
sometimes to pressure, sometimes to contraction of the affected parts, but
especially to hæmorrhages, and not infrequently are followed by a fatal
termination.

II. NEW-FORMATION OF ENDOTHELIUM.

HIS, *Die Häute u. Höhlen des menschl. körpers.*, 1865.—RINDFLEISCH, *Virch.
Arch.*, 1862, XXIII., p. 523 ; *Lehrb.*, p. 201.—The numerous and more recent works
on connective tissue and lymphatic vessels.

ENDOTHELIUM forms either the internal surface of saccular or tube-like
expansions of connective tissue ; or it lies between the bundles of looser

connective tissue. In the former locality it is represented by a connected single layer of flattened (poor in protoplasm), rarely rounded, for the most part 5–6 sided cells. To these belong serous sacks, articular capsules, mucous bursæ, also the endocardium, blood- and lymph-vessels, the wall of the blood- and lymph-capillaries. In the last the endothelia are the former-ly described fixed connective tissue corpuscles. Endothelium has its origin neither from the external nor from the internal germ-layer, like true epi-thelium, but like all connective tissue and vessel-elements from the middle germ-layer.

According to the experimental and pathologico-anatomical observations of KUN-DRAT and DURANTE (s. p. 250), as well as of WALDEYER (*Virch. Arch.*, XL., p 379), the endothelium of the vessels and serous membranes may, during a state of irrita-tion, send out fibrillar processes which coalesce with one another.

A new-formation of endothelium occurs in form of regeneration, hyper-trophy and tumor. It affects either only endothelium, or at the same time the subjacent connective tissue.

A. REGENERATIONS OF ENDOTHELIUM.

These occur partially in most cases very often, partly after wounds, partly after inflammations, etc., perhaps as a physiological process. The more immediate histological conditions are unknown.

B. HYPERTROPHIES OF ENDOTHELIUM.

These occur rarely pure, almost always with those of the subjacent con-nective tissue.

PURE endothelial hypertrophies are sometimes found in hypertrophies of the skin, etc., in the lumen of normally wide or dilated, old or new-formed lymph-vessels. (See pp. 383 and 392.)

HYPERTROPHIES OF SEROUS AND SYNOVIAL MEMBRANES occur sometimes alone, sometimes simultaneously with inflammation (with so-called fibrinous exudation). They are represented either as milky or tendinous spots, and are then for the most part poor in vessels. Or they have the form of fila-ments, strings, membranes, etc., which consist of the same substance as the serous membranes themselves, and almost always of abundant bloodvessels (sometimes even lymphatic vessels and nerves). They occupy sometimes only one layer of a serous membrane, sometimes both, with consecutive growth of the same: so-called PSEUDO-MEMBRANES, ADHESIONS, SYNECHIÆ. (See p. 270.) The growth of serous sacs diminishes the free movableness of the affected organ, which for the most part is followed by diminished func-tion; those of the joints furnish the conditions of so-called ANCHYLOSIS.

The hyperplastic development of connective tissue in continued dropsical effusions proceeds in part from a moderate increase of thickness of the serous membrane, but especially from another character of their fibres; the latter are stiffer, less distensible, less affected by chemical reagents, with unequally increased refraction of light (so-called SCLEROSIS: VIRCHOW). For the latter reason they have a milk-white color. (RINDFLEISCH, *Lehrbuch*, 1 Ed., p. 218.)

HYPERTROPHIES OF THE ENDOCARDIUM (and of the valves of the heart), OF THE INTIMA OF THE ARTERIES, rarely of the veins, have for the most part the form of tendon-like deposits, rarely and only in the two former localities that of papillary excrescences. In the former form they constitute the most

essential change in the so-called deposit-process of arteries, and, after the appearance of fatty and chalky metamorphosis, etc., the so-called atheromatous process.

Many so-called valvular diseases of the heart arise without any inflammatory phenomena; perhaps they depend upon a hypertrophy of the connective tissue of the valves with consecutive cicatricial retraction.

The histological conditions of all these hypertrophies are essentially the same as hypertrophic formation of common connective tissue, but are not yet exactly known. Also cicatricial contraction not infrequently occurs, and in the valves of the heart is especially important.

Consult BUHL, *Ber. d. Bayr. Acad.*, 1863, II., p. 59.—RINDFLEISCH, l. c.—LANGHANS, *Virch. Arch.*, XXXVI., p. 187.
According to TRAUBE (-HERTEL, *Berl. klin. Wchschr.*, 1871, No. 30–32), arteriosclerosis depends upon a migration of colorless blood-corpuscles through the endothelium into the spaces between the striped lamellæ of the intima, and upon a metamorphosis of these into spindle-shaped and stellate cells.

Many hypertrophies of the endothelium and subjacent textures are represented as so-called DENDRITIC VEGETATIONS, *i.e.*, as for the most part small, hard, filamentous or villous formations, usually poor in vessels. They occur as the known arachnoidal tufts or Pacchionian granulations; also in serous membranes, especially the pleura, in joints, on the semilunar valves of the aorta and pulmonary artery. Most of the free bodies of the cavities of joints and the vaginal tunic of the testicle are in organic connection with those of the serous membranes, until this connection is finally dissolved.

C. AS TUMOR-LIKE NEW-FORMATIONS OF ENDOTHELIUM (if we exclude those of the vessels and vegetations) may be regarded many so-called anomalous mucous bursæ over the projections of the spine, amputation-stumps, club-feet, old luxations, etc. Also to this class belong many sarcomata and carcinomata, which arise from a growth of the endothelium of the lymphatic vessels.

According to BOLL (*Arch. f. micr. Anat.*, 1871, VII., p. 275), all, even the smallest clefts of connective tissue, are lined by endothelial flat cells, and form, so to speak, the smallest serous spaces. This explains the formation of accidental mucous bursæ and serous cysts in connective tissue.
Concerning the origin of accidental mucous bursæ, see VIRCHOW, *Geschw.*, L., p. 194.

III. NEW-FORMATION OF NEUROGLIA.

VIRCHOW, *Ztschr. f. Psych.*, 1846, p. 242; *Ges. Abh.*, pp. 688 et 887; *Arch.*, III., p. 245; V., p. 592; VI., p. 136; VIII., p. 540; *Die krankh. Geschwülste*, II., p. 123.—Observations by WEICKERT, SCHÜPPEL, and others.—Consult also the works of BIDDER and KUPFER, STILLING, LENHOSSEK, JACUBOWITSCH, GOLL, FROMMANN, FREY, DEITERS, GERLACH, MEYNERT, BOLL, and others.

NEUROGLIA, NERVE-CEMENT is the connective-tissue-like substance, which in the brain, spinal cord, and in the nerves of higher sense forms a for the most part very delicate net-work, in the spaces of which lie the nerve-fibres and ganglion-cells. This is according to the locality sometimes denser, resembling a nucleated connective tissue net-work (thus in the ependyma of the ventricles of the brain); but sometimes and most frequently it is so soft that it appears entirely amorphous or finely granular. In the latter case

there lies in a for the most part very scanty basis substance, exhibited only by hardening in alcohol, etc., a very fine net-work, rounded or spindle-shaped or branched cellular parts, which, however, are so brittle that they for the most part appear only as nuclei.

The NEW-FORMATION OF NEUROGLIA is diffuse as hypertrophy, and occurs in form of tumor. Its regeneration is not certainly known.

A. DIFFUSE HYPERTROPHY OF NEUROGLIA.

This is often found in the ependyma of the ventricles as an uniform or granular hypertrophy of it; it is more rarely extended over the whole brain or only over some sections of the brain, as so-called cerebral hypertrophy (interstitial hyperplasia).

Hypertrophy of neuroglia occurs from various, quite unknown causes, mostly with change of the same. The neuroglia either increases simply in quantity, its character is unchanged; or its nuclei are increased to various extents; or it is translucent like horn, grayish-yellow, like dull glass, stiff; or, finally, it is more or less distinctly FIBROUS. The nerve-fibres, the processes of the ganglion-cells and the cells themselves, remain therein sometimes normal, sometimes they are separated from one another, deprived of their contents, etc. At the same time granular cells often arise, corpora amylacea, pigment-masses. The affection is acute, sub-acute, and chronic. It affects chiefly the ependyma, the medullary substance of other portions of the brain, the medulla oblongata, the spinal cord. It is met with in the various forms of so-called hypertrophy of the brain and spinal cord, in so-called SCLEROSES, indurations, and many atrophies of these; in the parts of brain surrounding tumors, also in paraplegiæ and general paralyses, especially in paralytic imbecility, in many chronic diseases of the mind, etc. (ROKITANSKY, *Lehrb. d. path. Anat.*, II., p. 430.)

B. NEUROGLIA-TUMOR, GLIOMA.

This consists of neuroglia without participation of nervous elements. It is found oftenest in the brain, especially in the medullary substance of the posterior and anterior lobes, as well as on the surface of the cerebrum and in the ependyma of the ventricles (here especially in chronic hydrocephalus). It forms for the most part single, rarely multiple, sometimes small (especially on the ependyma), sometimes large (of the size of the fist and larger) tumors, which are usually not sharply defined; they are mostly very soft, easily crushed, of an appearance like that of the cerebral medulla, more rarely of a reddish color; they are rarely (especially on the ependyma) throughout solid or only in the centre, even as hard as cartilage, without vessels. These distinctions depend upon the relation of the cellular elements to the intermediate substance, as well as upon the vascularity: SOFT, RICH IN CELLS, medullary—HARD, FIBROUS—TELEANGIECTATIC GLIOMA.

The MICROSCOPE shows the characters of normal neuroglia; besides these often occur, especially around the vessels, long, fibre-like cells, as well as (in the ependyma) corpora amylacea.

CEREBRAL GLIOMATA never extend to the cerebral meninges. They are sometimes congenital, sometimes the result of injuries.

The first GROWTH of cerebral glioma is mostly slow and without symptoms. Also its farther course is mostly slow, except with increased vascularization. The consequences of cerebral glioma are, besides those common to every other tumor: congestions with symptoms of cerebral pressure or cerebral irritation; apoplectic phenomena; dropsy of the cerebral ventricles (in consequence of pressure on the veins).

The METAMORPHOSES of glioma are: hæmorrhages; fatty metamorphosis of cells, whereby sometimes cavities, like foci of yellow cerebral softening, sometimes cystoid spaces arise; ossification. Healing is perhaps possible through fatty degeneration.

Gliomata show in part COMBINATIONS with other new-formations, especially sar-

coma and myxoma; in part TRANSITIONS to myxoma (myxo-glioma), to fibroma (fibro-glioma), to partial scleroses of the cerebral substance (ROBIN'S scleroma). Their external appearance may, according to the kind of glioma, bear a similarity to acute encephalitis (red softening of the brain), to simple cerebral hæmorrhages, to yellow softening, to sarcoma, tubercle, cancer, etc.

To the gliomata belong, according to VIRCHOW (*Die krkh. Geschw.*, II., p. 148), perhaps also: the so-called hyperplasiæ of the pineal gland; the partial hyperplasiæ of the medullary substance of the supra-renal capsules; some congenital sacral tumors; some tumors of the nerves of higher sense, especially of the auditory; some tumors of the retina, but which afford in part transitions to sarcoma and medullary fungus; some so-called medullary tumors of the kidneys, which occur sometimes with interstitial nephritis.

IV. NEW-FORMATION OF FATTY TISSUE.

WEIDMANN, *De steatomat.*, Mainz, 1817.—FÖRSTER, *Virch. Arch.*, 1857, XII., p. 197.—FÜRSTENBERG, *Die Fettgeschwülste der Thiere*, etc., 1851.—VIRCHOW, *Arch.*, 1855, VIII., p. 537; XI., p. 281; *Die krkh. Geschw.*, I., p. 364.—CZAJEWICZ, *Arch. f. Anat., Phys.*, etc., 1866, p. 289.—FLEMMING, *Arch. f. micr. Anat.*, 1870, VII., p. 82.—TOLDT, *Wien. acad. Sitzgsber.*, Juli, 1870.—VOIT, *Z. f. Biol.*, 1866, II., pp. 6, 189, et 307.—HOFMANN, *Ib.*, 1872, VIII., p. 153.—TOMSA, *Arch. f. Dermat. u. Syph.*, 1873, V., p. 1.

NEW-FORMED FATTY TISSUE is, like normal fatty tissue, represented by connective tissue, whose corpuscles are transformed, by the taking up of fat, into large, round, spherical cells. New-formed fatty tissue proceeds only from fatty or connective tissue (or from mucous tissue). It consists of a vascular framework of connective tissue, poor in connective-tissue corpuscles and elastic fibres, which, as in normal fatty tissue, forms lobules or is clustered, and of the therein stored fat-cells.

According to RANVIER (*Compt. rend.*, 10th July, 1871), fat-cells are, by injection of acidulated solution of nitrate of silver (1 : 1000) into the subcutaneous fat-tissue, divided into three parts: an enveloping membrane, a thin protoplasma-layer with lenticular nucleus, lying immediately against the membrane, the central fat-drop. By imagining the latter absent, there is left a flat cell similar to common connective-tissue cells.

New-formation of fat-cells rarely takes place by division of the original fat-cells, but from the original or by division of the multiplied corpuscles of connective or mucous tissue, by absorption of fat. New-formed fat-cells are, like those of young individuals, at first small; later they become larger, like normal fat-cells; at the same time the old fat-cells are almost always greatly enlarged. New-formation of connective tissue and vessels follows in the usual manner.

The mode by which fat enters the cells has been exposed by FLEMMING as follows. The fat or fat-furnishing material circulates in the blood in the form of a dissolved compound, and transudes also in this form. If the solution leaves the vessel, it becomes decomposed, and fat is precipitated : thus free fat-drops in the tissue. Where a cell-body is saturated by the solution, fat is precipitated in it, perhaps with especial energy, and where this continues there is formed a fat-cell. The fixed cells of the adventitia of the vessels and the fat-cells there to be found, accidentally also some migratory cells, are at first continuously bathed in this solution. That the fat deposit always occurs only in small areas, is probably due to local dilatations of vessels : from these transudation is greater than from narrower vessels, on account of the retardation of the current in the former. This view is favored also by the relatively large number, and the almost constant occurrence of migratory cells in the vicinity of the fat-forming areas.

New formation of fat-tissue is often observed, and in various forms.

A. Regeneration of fatty tissue

occurs with extraordinary frequency. It consists in the new-formation of all its elements. This has not yet been especially demonstrated, but with great probability is conjectured from the external condition of cicatrices of fatty parts. It is, however, at all events only slight.

Or, regeneration affects only the fat, while the remaining elements (cell-membrane, with nucleus, connective tissue, and vessels) are preserved. This occurs after common acute or chronic emaciations, in the subcutaneous, etc., fatty tissue, as well as in the cavities of the body and fat-containing marrow of bones. In these cases the cells, simply atrophic or filled with serum, are again filled with fat. If in the meanwhile the connective tissue also is metamorphosed into mucous tissue, the latter again becomes fibrous.

B. Hypertrophy of fatty tissue

is sometimes circumscribed, representing gradual transitions to fatty tumor, sometimes generally distributed over the whole body.

a. Circumscribed, non-tumorous hypertrophy of fatty tissue,

occurs most often as a secondary process in the vicinity of and within atrophic organs, e.g., on one or both kidneys (in atrophy after pyelitis, in so-called granular atrophy); in the medulla of bones, where it forms to a certain extent the normal process of age, and also in bones not at all or little used; in the muscles of one or more members, as so-called muscular hypertrophy (*lipomatosis musculorum progressiva*).

In bones, atrophy of the bone-tissue is always the primary, fat-increase the secondary affection. In very rare cases there occurs a pathological so-called hypertrophy of the muscles of the extremities with diminished function. This depends only upon a diffuse new-formation of fatty tissue between the muscle-elements, with gradual destruction of the latter. (Griesinger, *Arch. d. Heilk.*, 1865, VI., p. 1.—Seidel, *Die Atrophia musc. lipom.*, 1867.—Barth, *Arch. d. Heilk.*, 1871, XII., p. 121.) According to Knoll (*Oestr. Jahrb.*, 1872, p. 1), lipomatous muscular atrophy consists in considerable fatty or connective-tissue growth of the interstitial muscular tissue, in hypertrophy of single, and in simple, fatty, etc., atrophy of many muscle-fibres. With Duchenne, Knoll calls the disease pseudo-hypertrophic paralysis.

These cases form the transition from fatty-tissue hypertrophy to fatty tumor, where the fat around an organ increases and thereby forms a tumor, which appears to belong to the organ as such: lipoma capsulare. Examples are afforded by the intra-orbital fat-tissue, fat in the vicinity of the pericardium, kidneys, especially in atrophy of the latter, fatty tissue hypertrophy of the normal, or enlarged, or atrophic (by inflammation or scirrhus) female mamma, similar hypertrophy in lymph glands; also fatty-tissue hypertrophy of the omentum in a hernial sac (omental lipoma), the same in the course of hernial sacs, but without the presence of a hernia, hypertrophy (so-called hernia lipomatosa), as well as fatty-tissue growth in the vicinity of a hernial sac (*lipoma herniosum capsulare*).

Fatty hernia (liparocele, hernia adiposa) is a circumscribed fatty tumor, for the most part enveloped by a membrane, which by its locality, mode of origin, etc., resembles intestinal hernia, and proceeds either from the sub-peritoneal connective tissue or is immediately connected by a pedicle with the peritoneum, and is usually pressed through one of the known hernial openings, most frequently through the linea alba. Fatty herniæ have their origin either from the metamorphosis of a primary hernial sac, or they are not connected with it, but in form and character resemble a hernia,

or they are the cause of the secondarily formed protrusion of the peritoneum. (WERNHER, *Virch. Arch.*, 1869, XLVII., p. 178.)

b. OBESITY, PIMELOSIS, polysarcia, *lipomatosis universalis*.

The CAUSES of obesity are partly predisposing, partly exciting.

Among the PREDISPOSING causes the most important is hereditary disposition: it is manifested sometimes already in the earliest years of life, sometimes after the twentieth, most frequently about the fortieth year. The determining causes are, on the one hand, increased supply of nutritive material, especially with a preponderance of vegetable and fatty food, often at the same time with the free use of spirituous liquors; on the other hand, lessened consumption of the body (bodily rest, phlegmatic temperament).

The determination of the causes of obesity, since these as so-called FATTENING are physiologically and agriculturally important, has during the last ten years called forth many works. This began with LIEBIG'S demonstration that in the feed of cows, geese, etc., there was not enough fat to furnish that secreted with the milk or the fat which had been deposited. That a food abundant in fat, whether the source of the fat is animal or vegetable, induces obesity, is firmly established: and yet the more immediate conditions are still not entirely and with certainty known. According to many (TOLDT, SUBBOTIN, and others), a direct passing of fat in an unchanged state out of the intestinal canal into fatty tissue does not take place; but all fat has its origin from the albumen consumed. For, since the blood never takes up a considerable quantity of fat, ALL the fat taken up from the intestine must always be consumed; the excreted carbonic acid must then correspondingly rise and fall with the amount of fat in the food. But RADZIEJEWSKY'S observation, that none or only a trace of foreign fats, not occurring in the organism, is deposited, if even the feeding had been continued for a long time, cannot be extended to the fats commonly found in animal bodies. A certain quantity of the latter remains in the body, dependent upon the size of the daily supply and the consumption during rest or work. Thus the fat of the food contributes to the fatty state of the animal organism (HOFMANN). Besides, fat reduces the consumption of albumen and limits the taking up of oxygen.

It is farther established, that the surplus of animal and vegetable albuminates taken up leads to fat-formation (HOPPE, PETTENKOFER-VOIT, KEMMERICH, SUBBOTIN, HOFMANN). This probably occurs by their being divided into non-nitrogenous (fat, sugar) and into nitrogenous complex atoms; the latter are converted into urea, etc., especially in the urine, while the former partly are oxidized to become carbonic acid and water, partly—on account of the want of oxygen—remain as fat in the body. Proofs for this fat-formation are furnished by fattened animals and milking cows; the fat and albumen of the nutriment supplied is not sufficient to afford the fat, or milk. (See also p. 301.)

Physiological and chemical proofs of the formation of fat from the hydro-carbons (LIEBIG) are wanting. Sugar, starch, etc., are, however, indirectly important with respect to the formation of fat, whilst they oxidize more easily than fat, and thereby the fats formed from the albuminates are protected from decomposition (PETTENKOFER-VOIT), whilst in the working animal they are oxidized, and thereby furnish the increased warmth given off during work.

Fat in obesity increases first in all parts where fatty tissue is found normally: most abundant in the subcutaneous tissue, especially of the abdominal region, in the omentum, mesentery, about the kidneys, in the pericardium, etc. Only later are fat-deposits also found in those parts where little or almost no fat is found: between the muscles and muscle-bundles, under the endocardium, etc. Many of these places show never or only in very slight degrees an increase of fat: thus the eyelids, the skin of the external ear, penis, scrotum. Of the glandular organs proper the liver often, sometimes the kidneys are infiltrated with fat. The new-formed fatty tissue effects the known changes of external form, and an increase of bodily weight to 100 and 150 kilo., in some cases to double of the weight.

The PHYSIOLOGY of obesity is still in many ways obscure. In a fat man the current of the nutritive liquid and the quantity of blood is less ; he takes up, on this account, less oxygen than a leaner person, and consumes less albumen, fats, and hydro-carbons. He thus needs for the retention of his size of body disproportionately less of these substances, and increases with a certain supply, when the leaner man decreases. Albumen and fat are not assimilated in the animal in proportionate quantities. In very adipose organisms the quantity of albumen to a high degree retrogrades. In them it happens that the store of albumen necessary for life sooner reaches its lower limit, and the animal dies from a want of albumen, while fat is still found in the body in massive quantities. In diseases, especially if they are attended by an increased transformation of albumen, these very fat persons resist for a much shorter time the consequences of diminished or lost appetite (albumen-inanition) than those who are leaner and have more abundant albumen, and often die without a sufficient explanation of death from the pathological appearances. ʻVOIT, l. c.—HOFMANN, l. c.)

According to TOLDT (l. c.), the fatty tissue of vertebrate animals is an organ of peculiar kind, and can neither by development, nor by histological behavior, nor by function be ascribed to connective tissue. This is taught partly by comparative anatomy, partly by the independence of the system of bloodvessels supplying fatty tissue, partly by the constant freedom of many parts of the body from fatty tissue development, partly by the persistence of the protoplasm in the fat-cell, even in the greatest deposition of fat. According to T., the protoplasm of fat-cells has the capacity, under the influence of a more abundant supply of fat, to prepare in the same manner as gland-cells prepare their secretion ; and *vice versa*, if the consumption exceeds the supply in oxidizable substances, the fat-cell again consumes the fat contained in it, and allows the resulting products of metamorphosis to enter the blood. T. saw in many fatty-tissue cells poor in fat, removed from the frog during the spring, distinct amœboid movements.

The HISTOLOGY and development of fat in obesity have been made better known by the works of FLEMMING. According to F., fat-cells uniformly arise in fattened animals, nurslings, and embryos under the skin, in the mesentery, etc., from fixed connective-tissue cells. The fat-cell deposit takes place always in or closely upon the adventitia of already formed small bloodvessels (arteries, veins, and capillaries growing out from these) ; according to F.'s later accounts, also sometimes in cells which still belong to the vessel-wall and then are exfoliated from it. The fat-deposit takes place only in separate foci, *i.e.*, from isolated vessels. The fat accumulates almost always in the protoplasmic middle portion of the fixed cells ; their surface is contracted in extent by the fat, and their processes seem to disappear. Besides fat-drops there are found for the most part only one, but sometimes also two and even three cell-nuclei (division-forms of connective-tissue corpuscles). The appearance of fat in round and free cells (wandering cells) has been only occasionally observed. Transition-forms of these to fixed cells are doubtful. On the other hand, finely granular fat regularly occurs free in the tissue. F. assumes a specific development of fatty tissue from mucous tissue only in so far as the connective tissue of the embryo, containing mucin and rich in liquid and cells, is called mucous tissue.

The CONSEQUENCES of obesity consist in many cases in an undisturbed state of health, while later and especially during the operations of other causes, there appear diminished capacity of movement of the voluntary muscles, diminished activity of the apparatuses of circulation and respiration, not infrequently also of that of digestion. Only during the further progress here occurs, through disease of the vessels, various disturbances of the brain, through those of the kidneys corresponding disturbances of the urinary apparatus. Sexual activity is for the most part diminished. Resistance to causes of disease, and in diseases themselves, is less (see p. 54).

C. FATTY TUMOR, LIPOMA,

is for the most part sharply circumscribed, rarely diffuse. In the former case it forms a tumor varying in size, not infrequently voluminous, mostly hemispherical, flattened in parts subjected to pressure, and projecting, like polypi, on free surfaces (skin, gastric and intestinal mucous membranes, joints), and which is distinguished from the surrounding structures by a

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distinct capsule. The surface of the tumor is regular or variously lobed. The cut surface shows fatty tissue, which is for the most part distinguished from normal fatty tissue only by the considerable size of the fat-cells, and is separated by vascular connective-tissue planes into divisions or lobes, varying in size, rounded or angular. Sometimes the fatty tissue is firmer than normal, which depends only upon a more abundant development of connective tissue : FIBROUS OR HARD LIPOMA, so-called STEATOMA. At other times the fat preponderates over the other elements : SOFT LIPOMA. In rare cases the vessels are very greatly developed : LIP. TELEANGIECTODES.

Lipoma occurs often. It is by far most frequent in the fatty subcutaneous cellular tissue, covered by relaxed skin (especially in the gluteal region, on the back, neck, axilla, anterior wall of the thorax, thigh), much more rare in parts wanting in fat, in intermuscular tissue and in fascia, not infrequent also on the inner surface of the joints, and in internal parts likewise containing fat-cells (greater omentum, mesentery, peritoneum, costal pleura, endocardium, lymph-glands, sub-mucous tissue, especially of the stomach and small intestines, rarely at the root of the tongue) ; rarely in organs wanting in fat (cerebral meninges, lungs, liver, kidneys, etc.) ; in pseudomembranes of the lungs.

Lipoma is mostly single, in rare cases multiple, never in the form of metastatic tumor.

FOUCHER (*Gaz. des hôp.*, 1863, No. 122) saw in a man, thirty-eight years old, four lipomata in the region of the neck, one on each side of the thyroid gland, one on the right, one on the left side in the region of the stomach, two in the lumbar region, two on the boundary between the latter and the sacral region ; all were perfectly symmetrical with respect to the two sides of the body.

The GROWTH of lipoma is slow, and is mostly central, rarely peripheral.

The CAUSES of lipoma are generally those which have been given. Lipomata are rarely found in childhood. Sometimes they are hereditary. They are acquired by irritations of every kind : in the skin, oftenest by pressure.

Mixed forms or COMBINATIONS with other tumors occur more rarely than pure lipoma : combinations with fibroma, cellular tissue tumor, myxoma, vascular tumor, cancer, cysts.

XANTHELASMA or XANTHOMA (*vitiligoidea, fibroma s. molluscum lipomatodes*) is a for the most part small, single, less prominent, yellowish tumor of the skin, most frequently of the eyelids, rarely of mucous membranes, consist of fibrous fatty tissue (or connective tissue containing fat).

RAYER, *Traité des mal. de la peau*, 1836 ; Atlas, Tab. VIII., Fig. 16. et Tab. XXII., Fig. 15.—AMMON, *Klin. Darst. d. Krankh., etc., d. menschl. Auges*, 1838–41, III., Taf. VI., Fig. 1.—ADDISON and GULL, *Guy's Hosp. Rep.*, 1851, VII., 2 Ser., p. 265 ; 1852, VIII., 1 Ser., p. 149.—ADDISON, *Journ. of Cutan. Med.*, 1868, VII., p. 268.—BÄRENSPRUNG, *Deutsche Klin.*, 1855, p. 47.—PAVY, *Guy's Hosp. Rep.*, 1856. —HEBRA, *Atlas d. Hautkrkh.*, 7. H., Taf. X.—NEUMANN, *Lehrb. d. Hautkrkh.*, 1870, p. 71.—WILSON, *On Dis. of the Skin.*, 5th Ed., 1863 ; *Journ. of Cutan. Med.*, 1867, I., p. 109 ; 1868, VI., p. 212 ; *Lect. on Dermatology*, 1871, p. 105.—MURCHISON. *Transact. of the Lond. Path. Soc.*, 1869, XX., p. 187.

According to KAPOSI-KOHN (*Wien. med. Wochenschr.*, 1872, No. 8 et 9), xanthoma (xanthelasma, vitiligoidea) is either in the form of spots (diffuse) or of small knots (tuberous). The former forms irregularly formed, sharply defined, small (to the size of a dollar) yellowish spots on the skin, which are flat or in places nodular, and are sometimes painful. They are found mostly in the eyelids, more rarely on the parts bordering on these, on the nose, external ear. Nodular xanthoma forms nodules like millet seeds or grains of wheat, whitish or yellowish, isolated or in groups, projecting

not above the skin or from two to four mm., which can be secured with the skin be-
tween the fingers. They are found more frequently on the cheeks, external ear,
especially on the palm of the hand along its normal furrows and lines, on the sides of
the phalangeal joints, etc.; also on the mucous membrane of the lips and cheeks,
nose, gums They are usually little, sometimes very sensitive to pressure. Xanthoma
undergoes no farther change.

According to WALDEYER (*Virch. Arch.*, 1871, LII., p. 318), xanthelasma of the eye-
lids consists not in a diffuse, but grouped considerable increase of the connective-
tissue bodies about the hair-follicles, sebaceous glands, sweat-glands, vessels and
nerves, in less degree also between the stronger connective tissue trabeculæ, and in a
fatty degeneration of all these new-formed cells. The fat is less finely granular, but
easily coalesces into larger drops. Likewise VIRCHOW (*Ib.*, p. 504) and MANZ (*Kl.
Monatsbl. f. Augenh.*, 1872, p. 251) —GEBER and SIMON (*Arch. f. Dermat. u. Syph.*,
1872, IV., p. 305) did not in a case find this structure, but (like HEBRA and others) a
hyperplastic development of sebaceous gland cells.

HUTCHINSON (*Transact. of the Med.-Chir. Soc.*, 1872, LIV.) has in forty of his own
and in seven other cases investigated the connection of xanthelasma of the eyelids
with other affections of the organism : in fifteen there were severe, in six lighter
habitual pains in the head ; often still other and less frequent nervous phenomena ;
in general extension of the spots there were found severe affections of the liver
(which had already been noticed by ADDISON).

The rare METAMORPHOSES of lipoma seldom affect the whole tumor, for the
most part only isolated portions of it. They are : spontaneous retrogres-
sion ; inflammation, sometimes with consecutive connective-tissue hyper-
trophy, more rarely with formation of abscess ; softening ; mortar-like or
stony calcification of the connective tissue ; transformation into mucous
tissue, especially in large pendent lipomata, etc.

Polypous lipomata of the skin, joints, and serous membranes may after atrophy of
their pedicle, become free : many so-called free articular bodies have a like origin.

V. NEW-FORMATION OF ELASTIC TISSUE.

NEW-FORMED ELASTIC TISSUE has either the form of common fine or
coarse elastic fibres, which show rectilinear borders, which are more rarely
dentated, or even provided with longer or shorter pointed processes ; or it
has the form of elastic membranes. Elastic tissue occurs rarely by itself:
as hypertrophy of the elastic tissue of the superior tracheal mucous mem-
brane, pulmonary pleura, arteries, never as a tumor proper.

A new-formation of elastic tissue is often found SIMULTANEOUSLY WITH
NEW-FORMATION OF OTHER TISSUES, almost constantly with that of connec-
tive tissue : in pseudo-membranes and adhesions of serous membranes, in
some connective-tissue hypertrophies, in sclerosis of the brain, in connec-
tive-tissue tumors of every kind, especially in fibromata and cysts, in sarco-
mata.

In scleroderma FÖRSTER and AUSPITZ found a moderate, ARNING a very
important increase of the elastic tissue of the corium, as well as of the
affected portions of the mucous membrane. I saw a new-formation of
abundant elastic tissue in a peculiar cerebral tumor.

The GENESIS of elastic tissue is unknown. According to DONDERS, VIR-
CHOW and others, elastic fibres arise through growth and union of connec-
tive-tissue corpuscles, while H. MÜLLER, HENLE, REICHERT, KÖLLIKER and
others assume that they are formed by an especial metamorphosis of gela-
tine-forming basis substance of connective-tissue deposits. According to
HERTWIG (*Arch. f. micr. Anat.*, 1872, IX., p. 80) the protoplasm of cells
forms the elastic substance, just as it, *cet. par.*, forms connective-tissue fibres.

The growth of elastic fibres once formed follows by intussusception into the extra-protoplasmatic substance.

VI. NEW-FORMATION OF OSSEOUS TISSUE.

DE HEIDE, *Exper. circa sanguinis missionem, etc.*, 1686.—DUHAMEL, *Hist. de l'acad. r. d. sc.*, 1741–43.—J. HUNTER, A Treatise on the Blood, Inflam., etc., Phila., 1796.—MIESCHER, *De inflammat. ossium*, 1836. — WATSON, *Edinb. Jour.*, April, 1845.—SHARPEY, *Quain's Anat.*, 5th Ed., II., p. 146, 1846.—KÖLLIKER, *Mitth. d. Zür. naturf. Ges.*, 1847, p. 93.—FLOURENS, *Théorie expériment de la form. des os.*, 1847.—GERLACH, *Ztschr. f. rat. Med.*, 1847, VI.—VÖTSCH, *Heilung der Knochen-brüche per primam intent.*, 1847.—VIRCHOW, *Arch.*, 1847, I., p. 136; V., pp. 172 et 409; WÜRTZL, *Verh.*, II., p. 150; *Die krankh. Geschw.*, II., p. 1.—SYME, *On the Power of the Periosteum to Form New Bones*, 1848.—STEINLIN, *Ueb. d. Heilungspr'e, nach Resect. der Knochen*, 1849.—HILTY, *Ztschr. f. rat. Med.*, 1850, III.—H. MEYER, *Müller's Arch.*, 1849, p. 292; *Ztsch. f. rat. Med.*, N. F., III., p. 143.—A WAGNER, *Ueb. d. Heilungsproc, nach Resect. und Exstirp. d. Knochen.*, 1853.—R. MAIER, *Das Wachsthum der Knochen nach der Dicke*, 1856.—HEIN, *Virch. Arch.*, 1858, XV., p. 1.—SCHWEIGGER-SEIDEL, *Disquis. de callo.*, Hal., 1858.—OLLIER, *Gaz. méd.*, 1858. *Journ. de physiol.*, 1859–63.—H. MÜLLER. *Ueber die Entwickelung der Knochensub-stanz*, u. s. w., 1858.—LIEBERKÜHN, *Arch. f. Anat.*, u. s. w., 1860, p. 824; 1862, p. 702.—VOLKMANN, *Virch. Arch*, 1862, XXIV., p. 512. — GEGENBAUER, *Jen. Ztschr.*, 1863, p. 1, III., p. 54.—BUCHHOLZ, *Virch. Arch.*, 1863, XXVI., p. 78.—NEUMANN, *Beitr. z. K. des. normalen Zahnbein- und Knochengew*, 1863; *Arch. d. Heilk.*, 1870, XI., p. 414.—WOLFF, *Arch. f. klin. Chir.*, 1863, IV., p. 183; *Berl. klin. Wschr.*, 1869, No. 46.—WEGNER, *Virch. Arch.*, 1872, LV., p. 11.

NEW-FORMED OSSEOUS TISSUE has on the whole the same properties as the normal tissue. It is either compact, or spongy, or shows various transitions of consistence. The periosteum is like the common periosteum of adult or young individuals. The same is true of bone-marrow, where this is present. The structure of new-formed bone often shows no deviations from normal osseous tissue. At other times the basis substance is irregularly lamellar, or fibrous, or entirely homogeneous; the bone-corpuscles are often irregularly distributed, not infrequently of varying size and form, but almost always in varying degrees stellate; the vessels are often numerous, less regularly distributed, of varying diameter.

There are two kinds of compact osseous tissue. The one corresponds to the common cortical substance of tubular bones; it is formed by the filling of the medullary spaces with concentric lamellæ of osseous tissue, which proceed from progressive ossification of the medulla: OSTEO-SCLEROSIS. The other corresponds to the cement-substance of teeth; it is formed by deposit of parallel layers of osseous tissue upon the surface, which proceed immediately from the periosteum or surrounding connective tissue: EBURNATION. Sclerosis is a secondary, eburnation a primary process. (VIRCHOW.)

OSTEOID TISSUE is a tissue which resembles normal osseous tissue only externally, but has not its essential histological and histo-chemical properties: its basis substance is strongly refractive, dense and homogeneous, but always yields gelatine; its corpuscles are often rounded, provided with very short processes; they are either the original connective-tissue corpuscles, or their origin is by division of these.

The CAUSES of osseous new-formation are for the most part known: exercise chiefly, often repeated irritations, as at the points of attachment of muscles and tendons to bones: so called physiological hypertrophy; congestive and collateral hyperæmia, as under bone-ulcers, in the neighborhood of inflamed, carious, etc., parts; wounds of every kind; inflam-

mations, especially chronic: so-called ossifying parostitis, periostitis, ostitis and osteo-myelitis; inflammations of the joints, of the surrounding soft parts chiefly, e.g., ossification of the cartilage affected in chronic inflammations of the mucous membranes of the air-passages, pleuræ; old age. Of the specific causes of osseous new formation there are to be mentioned: constitutional syphilis, as consequences of which there arise thickenings, etc., of various bones, and according to the older clinical, as well as the more recent experimental investigations, phosphorus. The causes of puerperal osteophytes, of most bony tumors, etc., are unknown.

Since the introduction of PHOSPHORUS into industrial art (especially the manufacture of matches) there has been known a peculiar disease of the lower jaw resulting finally in necrosis, in which there arises a simultaneous formation of new bone from the periosteum, which in all essential points resembles the old. WEGNER by experiment farther confirmed the bone-forming action of phosphorus. By the direct local action of phosphorus vapor on the periosteum of the lower-jaw as well as on that of other bones in rabbits there may be excited a disease wholly analogous to the known periostitis of the inferior maxilla, with moderate new-formation of bone and necrosis. As in man the poison for the most part enters demonstrably through a carious tooth, so also in rabbits is a wound of the soft-parts and periosteum necessary. W. has farther shown, that after the use of minimum doses of phosphorus for weeks or months in rabbits, dogs, cats, fowls, there is developed more distinctly in growing than in fully-grown animals, especially where spongy osseous substance is developed physiologically from cartilage, uniform, compact bony masses similar to the compact surface of bone. Their origin from cartilage is like that of normal bone, except that the greatest part of the proliferating cartilage-cells is not transformed into medullary cells but into bone-corpuscles. Finally the anomalous formed bony substance yields to the same physiological wasting like the normal bone. If the feeding of phosphorus takes place with intervals of abstinence, then there are found proceeding from the intervening cartilage alternate layers of condensed compact and common substance with broad meshes. Essentially the same, but macroscopically and microscopically not so easily recognizable, is the modification of periosteal apposition-processes in tubular as well as in flat bones. Besides, the compact substance formed before the feeding is also sclerosed. Finally there occurs with the same circumference a greater thickness of the compact surface of the diaphysis at the expense of the diameter of the medullary cavity: the interior compact surfaces appear thus not as completely resorbed as normal. In adult animals this is much less striking, except in hens, in which after feeding with phosphorus for months there appears a real closure of the medullary cavity by true bone substance. Chemical analysis shows, that bones of animals fed with phosphorus nearly resemble normal bones in composition, and that the former contain no more phosphates than the latter. In experiments on the development of bone in fractures, subperiosteal resections and periosteal transplantations, W. found by phosphorus-feeding a more abundant, denser and more solid, probably also quicker development of bone.

According to MAAS (Tagebl. d. Naturf.-Vers., 1872, p. 171) the action of phosphorus is based on the withdrawal of a great quantity of oxygen from the blood: the same bone-deposits are formed by feeding with other means which withdraw oxygen, especially with the arsenic acids, as well as with pyrogallic acid.

A new-formation of osseous tissue serves as material for filling up after diminution or loss of the normal contents in complete or incomplete, non-reduced luxations especially of the hip-joint, after loss of the teeth in the alveoli, after loss of the eye in the orbit, in senile atrophy of the brain as so-called internal osteophyte.

The DEVELOPMENT of pathological osseous tissue takes place by far most frequently from normal or new-formed connective tissue, especially from the periosteum and indeed from normal connective tissue, as well as especially often from hyperæmic and inflamed (so-called *periostitis ossificans*), and from the bordering soft parts (so-called *parostitis ossificans*). Much more rarely does it arise from cartilaginous tissue. Perhaps it is formed sometimes also immediately, without preceding formation of connective tissue or

cartilage, from a soft very cellular tissue. It probably arises very rarely from pure osseous tissue; and yet accurate investigation is still wanting.

According to BILLROTH (*Oestr. Jahrb.*, 1869, XVIII., 4 et 5 H., p. 3) young osseous tissue has its origin in migrated colorless blood-corpuscles. In the bones of young dogs, which very soon after birth were repeatedly fed·with cinnabar, he saw it in the youngest formed bone laminæ, especially in the bone-corpuscles; likewise in the cartilaginous cells of the fracture-callus of young dogs.

Periosteum retains its bone-forming capacity even when it has been partly or wholly removed from the bone and transplanted into other parts of the body; but especially, what is especially important in resections of bones, if it is retained, while the bone is in any manner removed (by disease or surgically).

Many have accepted DUHAMEL's proposition: " *le périoste fait les os;* " while others sometimes refer to the bone an essential share in the formation of callus (MIESCHER, J. MÜLLER, SCARPA, SÖMMERING and others), sometimes ascribe an equal importance in that process to soft parts and bones (BRESCHET, CRUVEILHIER and others). B. HEINE studied in animals the healing process after resections. SYME, STEINLIN, A. WAGNER and others followed him. They came to the conclusion, that the periosteum surely plays the chief part in the reparation of bone-defects arising by resection, that nevertheless a reproduction of bone takes place also without periosteum, which proceeds from the medullary cavity or diploë, so far as they are injured, or from the soft parts surrounding the bones. FLOURENS later, after numerous experiments, became a defender of DUHAMEL.

OLLIER has experimentally shown, that pieces of periosteum, when completely separated from their original place and transplanted into other parts, retain their capacity of generating bone: so-called *ostéoplastie périostique*. If a bone, *e.g.*, the radius of a rabbit be partly cut out, and the periosteum left in place, there will be found after two months a new piece of bone, similar in form and character to the old. If, on the other hand, the periosteum be removed, there will scarcely be formed a trace of soft fibre, which at the most will contain some osseous nuclei or scales. The latter are usually derived from the remains of the periosteum left behind. The soft textures bordering on the periosteum possess no bone-generating properties. If the periosteum and superficial parts of the compact tissue of the diaphysis of a long bone be removed without opening into the medullary canal, the bone will be more slowly restored. Regeneration after preservation of the periosteum succeeds not merely in long tubular bones, but also in flat bones, *e.g.*, the scapula. If in the metatarso-phalangeal joints of the rabbit the synovial membrane and ligaments be preserved as far as possible, so that the latter remain in connection with the periosteum, there will be generated new portions of bone with a complete joint. According to O the epiphyses also of long bones are regenerated in rabbits, as well as short bones, *e.g.*, the calcaneus, os cuboideum. BROWN-SÉQUARD saw in guinea pigs regeneration of the posterior segment of the vertebral arch and of the spinous processes of four vertebræ. Regeneration of the epiphyses in man has been observed by TEXTOR and SYME in the elbow, by LÜCKE in the humerus.

GOUJON, *Journ. de l'anat. et de la phys.*, July, Aug., 1869) found in variously modified experiments on rabbits, doves and fowls, that the bone-marrow also takes part in the reproduction of bone-substance.

All these experiments are of direct utility in practical surgery. MALGAIGNE first laid down the rule, to preserve the periosteum as far as possible in resections (so-called sub-periosteal resections). Thus there arose as the special aim of conservative surgery so-called osteoplasty, in which is included all those operations, in which bone-substance itself or bone-generating tissue is implanted into a part of the body, in order thereby to effect the continuous existence of bone-substance in this part. Disregarding the older methods of operation of PIROGOFF, NÉLATON and others, the above proposition of OLLIER has, by B. LANGENBECK and others, been accorded its practical value: in rhinoplasty, wherein the pericranium is transplanted simultaneously with the frontal flap, in order thereby to generate in the new formed nasal bridge a new-formation of bone, for the regeneration of the defect of the bony portion of the nose; and in uranoplasty (loosening and shifting of the muco-perios-

teal covering of the palate) in order to close by new-formation of bone the fissure of the hard palate.

The HISTOLOGICAL CONDITIONS in pathological formation of bone are as follows: more accurate details, corresponding to the most recent investigations on normal ossification are yet for the most part wanting.

In the FORMATION OF OSSEOUS TISSUE FROM CONNECTIVE-TISSUE (and periosteum) there appears either no increase of connective tissue corpuscles, or such an increase does take place.

In the former case the connective-tissue corpuscles retain their spindle-shaped form; or they become stellate, the processes appear in communication with one another: OSTEOID TISSUE. In both cases, calcareous salts are deposited in the basis substance. This form of bone-formation occurs oftenest in ossification of tendons.

In the second case, the connective-tissue corpuscles (or the cells of the red medulla, or the fat-cells of the yellow medulla, after that they, by loss of their fat, have been metamorphosed into analogous corpuscles) increase by division, rarely by endogenous cell-formation. The connective tissue (or periosteum) partly hereby, partly through hyperæmia, new formation of vessels and consecutive soaking with plasma, becomes thicker and gelatinous. With respect to the new-formed cells, those separated from the old bone become connective tissue, vessels, fat-cells, or persist as simple medullary cells; those, on the other hand, lying nearest the bone are formation-cells of true bone-substance: so-called OSTEOGENIC CELLS or OSTEOBLASTS. They are more or less regularly arranged, like epithelium, on the surface of bones, and, according to one view, secrete a homogeneous basis substance, which becomes fibrous and in which calcareous salts are later deposited, while, according to the other view, the basis substance is a direct product of metamorphosis of the peripheral portion of the osteoblasts themselves. The osteoblasts or their remains become stellate bone-corpuscles.

In the FORMATION OF OSSEOUS TISSUE FROM CARTILAGE, either there is a SIMPLE DEPOSITION OF LIME IN THE BASIS SUBSTANCE OF THE CARTILAGE, as well as in the external membrane of the cartilage-cells (with peculiar laminar thickening on the interior of the corpuscles), and supplementary radiation of the internal membrane of the cartilage-cells: the former becomes the basis substance of the bones, the latter the bone-corpuscles. This process has been most frequently observed as a change incident to age, in the ossification of the costal and laryngeal cartilages, also in rachitic bones (where investigation is easy on account of the slight calcification), as well as in enchondromata. It is included in simple calcification of cartilage.

Or there occurs the following PROCESS, ANALOGOUS TO NORMAL OSSIFICATION OF CARTILAGE. At first the basis substance of the cartilage is calcified together with the cartilage capsules. Then there arises by progressive division of the cartilage-cells proper, one brood of young cells after another, while at the same time the calcified mass again disappears by absorption. These young cells become partly medullary and fat-cell, vessels, etc.; partly they represent osteoblasts, which change in one of the above-mentioned ways.

On the ORIGIN OF OSSEOUS TISSUE FROM BONE-SUBSTANCE, *vide infra*.

Young new-formed bone is usually very porous, and rich in vessels and medulla. Usually, only later does it resemble normal compact osseous tissue, whilst new bone-masses are deposited concentrically in the spaces of the porous tissue. But, then, compact osseous tissue often becomes porous again by resorption. Thus also the processes of pathological ossification herein resemble those of normal ossification.

The views respecting the very complicated processes of normal ossification are still at great variance. On the one side are SHARPEY, BRUCH, H. MÜLLER, GEGENBAUER, and LANDOIS, on the other LIEBERKÜHN, who assumes an immediate transition of cartilage into bone. The same opposition respecting the share of osteoblasts in the formation of basis substance exists between GEGENBAUER and WALDEYER.

The GROWTH of new-formed osseous tissue probably takes place in part like that of normal osseous tissue, from the surrounding connective, cartilaginous, or osseous tissue; it is in part interstitial. Bone increases in THICKNESS normally, by the continuous growth outward from the internal periosteum of new osseous tissue, while at the same time the medullary cavity is increased by absorption of the bone. This is in part shown by microscopical investigation, in part by experiment: a ring fitted around a long bone approaches the medullary cavity (FLOURENS' experiment). The normal growth of tubular bones in LENGTH takes place in the epiphysal cartilages. This is demonstrated partly by the microscope, partly by experiment. If pegs be inserted into the diaphysis of bones of growing animals, their distance apart in the diaphysis will remain the same, while their distance from the epiphyses corresponds with the growth of the bone in length (HUNTER's experiment). The existence of an interstitial growth of bone is from the more recent experiments in normal animals called in question. It probably occurs under pathological conditions. It is mainly INTERCELLULAR, through increase of intercellular substance; in fœtal life besides, it is also CELLULAR, whilst the bone-cells become larger or increase in the osseous tissue itself.

According to WOLFF (Berl. kl. Wschr., 1868, Nos. 6, 7, 10, and 14), growth in length of tubular bones is not exclusively dependent upon apposition in the diaphysal limits, but there is a true expansion of the already formed bone. W. found in numerous cases that the distance apart of two portions of wire, fixed in bones and bent at right angles, becomes greater during growth. From experiments on rabbits he estimates the interstitial growth of the human tibia at, at the least, 25 mm. If two fine holes be bored in the diaphysis of a young animal, and these connected by inserting the ends of a fine wire bent at right angles, there will after a time be a bending of the bone, whose concavity will correspond to the surface on which the wire lay. The growth of bone in thickness is, according to W., chiefly interstitial. Rings of metal wires fitted around the bone do not penetrate to the medullary canal, but where they are situated they cause a heading-in of the osseous tissue. The constriction of the ring, which prevents the normal expansion of the bone, produces a narrowing of the medullary canal. The metal ring lying in a notch of new-formed osseous tissue is grown over, whereby the ring seems to have migrated toward the medullary cavity. The bones, after feeding with madder for four days, received, not only on the external but also on the internal surface, an intense red color. According to W., the periosteum is of slight importance with respect to the growth in thickness of bone: on the twenty-eighth day after destruction of the whole periosteum of one tibia of a young rabbit no difference could be discovered between the bones of the operated side and those of the side which had not been operated on. WOLFF, in a later work (Berl. med. Ctrlbl., 1869, No. 54), regards interstitial growth the exclusive process of growth in bones; no apposition exists in the cartilage of the epiphyses, here cartilage is just as little metamorphosed into bone as that in the medullary cavity medulla arises from bone. Consult also WOLFF, Virch. Arch., L., p. 389.

Contrary to WOLFF and others, and in favor of the appositional growth of bones, are first of all PHILIPEAUX and VULPIAN (Arch. de physiol. norm. et path., 1870, No. 5 et 6, p. 551). LIEBERKÜHN (Marb. naturw. Sitzgsber., 1872, p. 40) has recently communicated experiments which confirm the apposition theory of HUNTER and FLOURENS, and show how also WOLFF's experiments are to be explained by it. Likewise MAAS (Arch. f. klin. Chir., 1872, XIV., p. 198). A ring placed around the tibia, under the periosteum, of a young guinea-pig, migrated in most cases toward the medullary cavity. The cases with apparent bending in of the bone substance were explained by M. by the fact that the surrounding ring, in part or throughout the whole circumference, prevented the activity of the periosteum. Also the super jacent layer

in the medullary canal is a sign of diminished activity : resorption of bone-substance is retarded at the point corresponding to the position of the ring. If pegs be introduced into auger-holes in the diaphysis of bones, their distance in the diaphysis will remain exactly the same : both pegs are separated by a distance corresponding with the growth of the bone in length from the epiphyses. M. never, like WOLFF, observed an increase of distance between the pegs. In many cases the experiment fails, whilst an osteoplastic periostitis (BILLROTH), or thickening of the diaphysis and elongation of the bone (LANGENBECK) arises, the latter perhaps in consequence of diminished activity of the epiphysal cartilage. If fractures be produced in the diaphysis, close to one of the epiphyses and the distance from the other epiphysis marked by a transverse ring fitted around the bone, the distance between the callus of fracture and the ring will remain the same : the callus like the ring, is separated from the epiphysis by a distance corresponding to the increase in length.

While all changes of form in growing bones are commonly referred to deposit at one point, and to absorption at another, the plasticity of osseous tissue, according to R. VOLKMANN, in connection with the changes of matter equalizing the tension, is in condition slowly to bring forth all the most important changes of form of bones. The pathological occurrences in this connection are : for the most part senile, sometimes also traumatic atrophy or interstitial absorption of the neck of the femur ; displacements of the articular extremities in consequence of increased pressure in *genu valgum et varum*, club-foot ; changes of form of the vertebræ and ribs in scoliosis, etc. ; displacements of articular surfaces in the same affections and in *arthritis deformans*, etc. Consult also HUETER (*Die Formentwickelung am Skelett des menschl. Thorax*, 1865). According to VOLKMANN (*Med. Ctrlbl.*, 1870, No. 9), intercalations in the epiphysal sutures are not, in the increase in length of large tubular bones, of much consequence. In fractures of the diaphysis, in extreme nearness to the joint, which are healed with such a dislocation that the seat of fracture can after years be determined with certainty, the point of fracture preserves, in spite of the increase of length of the bone, its old topographical relations to the joint. In exostoses, which are developed on the articular extremities of the diaphyses of young individuals, no change of deposit can likewise be demonstrated in the progressive increase of the bone.

THE HISTOLOGICAL RELATIONS OF INTERSTITIAL BONE-GROWTH are still little known. The irregularities so frequent in pathological bones in the arrangement of bone-corpuscles and basis substance, in lamellar systems, etc., stand probably in relation herewith. RUGE (*Virch. Arch.*, 1870, XLIX., p. 237) made experiments and measurements on interstitial growth of bone. The intercellular substance of bones increases directly with the age : the distances between the cells become greater, and in all directions ; the bone becomes thicker, broader and longer, it is expanded. The corpuscles themselves in extra-uterine life generally remain without measurable change, their breadth and thickness decreasing only a little with age. The distribution of the bone-corpuscles in growth of bone varies histologically. In general the corpuscles lying near the vessels, are elongated, while those more distant show no preponderance of a certain dimension. Excrescences are also found in young bone-corpuscles (in man from the third to the eighth year), from those of very small dimensions to the entire doubling of the corpuscles—thus manifest processes of division.

The METAMORPHOSES of new-formed osseous tissue are wholly like those of the normal tissue. The calcareous salts of bones are not so insoluble for animal fluids, that a continual (under abnormal conditions) increased metamorphosis cannot be assumed. The changes in question, aside from resorption and sclerosis, are inflammation, suppuration, necrosis, etc.

New-formation of osseous tissue occurs : as regeneration, hypertrophy, and tumor. An especial consideration is also due the metamorphosis of other kinds of tissue (connective tissue and cartilage) into bone.

A. REGENERATION OF OSSEOUS TISSUE is very frequent.

Its most common cause is fracture. It occurs also usually after wounds, by blows, gun-shot, after amputations, more rarely after trephining and resections, after extirpation of bones, necrosis, etc.

In all these cases there is a complete or incomplete reparation of the bone. Healing takes place either by first intention or after previous for-

mation of pus and granulations. In the former case there appears an in-
crease of connective-tissue corpuscles, especially of the periosteum, in less
degree of the Haversian canals and medullary substance, probably also of
the bone-corpuscles, and thereupon ossification. In the latter case a part
of the new-formed cells are again destroyed in form of pus-corpuscles ; very
vascular granulations arise, and from them, with cessation of suppuration,
osseous tissue.

In HEALING of FRACTURES regeneration of the bones takes place in the
following manner. The blood effused at the time of fracture probably does not
contribute to the formation of callus. A larger quantity effused hinders such
formation ; it disappears after previous metamorphosis into fat, pigment,
etc., by resorption. The periosteum takes the most essential part in the
production of callus ; it swells, alone or with the surrounding soft parts,
within the first days after injury in consequence of a thorough soaking with
nutritive liquid (from the hyperæmic vessels), and especially in consequence
of a great new-formation of formative cells, and retains a reddish, gelatinous
appearance. From it there arises the so-called PROVISIONAL or EXTERNAL
CALLUS. This callus forms around the point of fracture a kind of capsule
or ferrule. That the formation of callus does not necessarily depend upon
it is shown by the fact that callus appears also where the periosteum is
entirely or in part wanting, as in many tendinous and muscular insertions.
The medullary membrane and tissue also share in the formation of callus :
this forms the INTERNAL or MEDULLARY CALLUS, which is represented by a
solid, rod-like mass. And, in a very slight degree, the tissue of the vessels
of bone at the point of fracture have a share, probably also the osseous
tissue itself : it forms the MIDDLE or INTERMEDIATE or proper BONE-CALLUS.
In many cases a share in this formation is also assumed by the inter-mus-
cular and inter-fibrillar connective tissue, perhaps also the muscular tissue
itself, as well as (at the articular extremities) the cartilaginous tissue.

After the appearance of the above-described processes of osteoblast for-
mation and a new-formation of vascular, cellular, homogeneous connective
tissue, at points sometimes also of hyaline or fibrous cartilaginous tissue
(the latter is usually present only in fractures of the bones of animals),
calcareous deposit begins in the intermediate substance of the cells. This
takes place mostly in a reticular manner, so that there remain accumulations
of numerous, more or less regularly distributed non-calcified cells, which
give to the new-formed, still vascular bones a porous appearance. At last,
by progressive deposit of calcareous matter, especially in the intermediate
and internal, partly also in the provisional or external callus, solid bone-
substance is formed : DEFINITIVE CALLUS. A part of this is then RE-AB-
SORBED, so that finally the swelling at the point of fracture wholly disap-
pears, and a more or less complete medullary cavity is established.

In some cases these processes vary greatly with the kind of fracture
(complete or incomplete fracture ; fissure, infraction—transverse, oblique,
and longitudinal fractures—simple, multiple, splintered fracture) with the
extent of laceration of the periosteum, with the size of the dislocation, ex-
travasation, with the kind of bone, etc.

DUPUYTREN'S distinction into provisional and definitive callus is no longer author-
ized, except in so far as it expresses the difference between the two forms with respect
to mode, time, and place of origin. The distinction is better between external, in-
ternal, and intermediate callus. But in a histological sense the first, provisional, is
certainly in essence different from the latter, or definitive, callus.

After healing of fractures with great dislocation of the fractured portions, or after
complicated fractures, there not infrequently arises a voluminous and irregular callus,

which sometimes never retrogrades, or only incompletely (so-called luxuriating callus, *osteoma fracturæ*).

The formation of callus proceeds especially from the periosteum and surrounding soft parts, if the fractured extremities are displaced over one another. The medullary cavity then becomes closed with bone; a part of the compact substance of the ends of the bones, especially the sharp edges and points, are resorbed.

NIKOLSKY (*Virch. Arch.*, 1872, LIV., p. 81) has experimentally investigated the differences in the healing of fractures of bones, in various periods of age. He distinguishes three periods: 1, the so-called stage of granulations; 2, the transformation of the granulation tissue into fibrous tissue, rich in spindle-cells; 3, the so-called stage of proliferation, *i.e.*, the metamorphosis of spindle-shaped cells by division into osteoblasts. In old animals the duration of each period is very much longer, healing often reaches only the second, sometimes only the first period, there is formed at the point of fracture a false joint.

According to LOSSEN (*Ib.*, LV., p. 45), retrogradation of callus consists in a chronic rarefying ostitis in the histological sense, which, on the one hand, goes along with dilatation of the medullary canals and disappearance of the tela ossca; on the other hand, leads to a new-formation of vessels, which L., from their origin and function, designates resorption vessels. Herewith also an ossifying ostitis simultaneously runs its course, which always gives rise to new bone from the medullary tissue and hereby the remaining bone, and provides the "definitive callus" in a histological sense.

In the regenerated osseous tissue there is formed, either from the beginning or after a varying length of time, the same fine architecture, in correspondence with the mechanical conditions, as has in late years been demonstrated in normal bones.

Consult H. MEYER, *Arch. f. Anat. Phys. u. wiss. Med.*, 1867.—WOLFERMANN, *Ib.*, 1872, p. 312.

According to J. WOLFF (*Arch. f. klin Chir.*, 1872, XIV., p. 270), in bones which are bent through pathological conditions (fractures, rachitis), but with this bending again in part or wholly capable of function, there is a change of the internal architecture corresponding with the changed form of the bone, and the changed claim of the single particles of bone dependent thereon. In fractures there is a complete revolution not only at the point of fracture, but to a great distance from it above and below: the trabeculæ arranged by the fracture in a statically unfit layer disappear and suitable new ones arise in their place. Thereby there is formed at the point of the callus a new bone-substance, with a wholly adapted architecture. Healing of fractures therefore consists of two processes perfectly independent of each other: of the inflammatory, transitory formation of callus at the point of fracture, and of the static, persistent new-formation, or solution of bone-substance at the point of fracture and apart from it. The latter processes are slight in fractures with slight dislocation, large in those with more considerable dislocation.

Also MARTINI (*Med. Ctrlbl.*, 1872, No. 37) has made valuable observations on the architecture of pathologically changed bones and joints. Likewise KÖSTER (*Würzb. Verh.*, June 15, 1872) has accurately described the architecture of bony anchyloses, especially of the knee and hip-joints.

In HEALING OF RESECTIONS there arises either a bony anchylosis, which in the knee-joint and the joints of the foot is desirable; or there appears a more or less perfect mobility. For the most part, then, the resected articular extremities, which sometimes also in form resemble the old extremities, are so loosely connected by fibrous bands that quite a mobility results. (In rare cases a true joint is formed, with articular cartilage, joint-cavity, and capsule.)

REGENERATIONS OF WHOLE BONES ARE RARE.

In my possession is the clavicle of a woman, which forty-five years before was separated by suppurative inflammation: a new clavicle was formed, which has nearly the form of the old bone and performs a normal function.

B. Hypertrophy of osseous tissue.

This occurs partly pure in various ways, partly in transitions into bony tumor, from various causes.

a. Hypertrophy of bone (in the narrower sense) is total (giant-growth), or partial, sometimes congenital (fingers and toes), sometimes acquired (normal prominences of bones at points of muscular attachment in men who labor hard, of the skull in hydrocephalus).

The common *genu valgum, e.g.* of bakers, arises through excessive growth of the internal condyle of the femur : this comes from the want of resistance exercised by the corresponding portion of the tibia, during standing for hours at a time with bent knees.   (Thus is explained also the excessive growth of a tooth, when the opposite one is absent.)

b. Elongation of bones occurs only in large tubular bones : spontaneously, in osteomyelitis, after necrosis, fractures ; sometimes in amputation-stumps, or in large ulcers of the feet.

c. Hyperostosis of bones, *i.e.* increase of diameter, occurs either in the whole bone, except at the suture or joints, or only in a part of it (periostosis).   It affects either only the external compact tissue (external hyperostosis), or only the medullary substance (internal hyperostosis or sclerosis), or both at the same time.

d. Osteophyte, *i.e.*, an osseous new-formation firmly attached to the surface of bones, but distinguished from the bone by its for the most part spongy texture (at least at the beginning) and its great vascularity ; occurs as a bony-mass, which is either diffuse, velvety, or laminated with splinters, or warty and in form of a stalactite, or spinous or cauliflower-like, or as an osteophyte in form of a bony mass which had been poured over the bone and become rigid during the flow.   Osteophytes in the earlier stages consist of reticular osseous tissue, the wide spaces of which contain in the centre a vessel, in the remaining space fibrous tissue.   In its further progress the bony mass increases mostly in concentric lamellæ, decreases in the inclosed mass, until finally only the vessel is present (hardening of osteophytes). Thus either they remain permanent, or there appears in turn, like the normal formation of a medullary space, a dissolution of the osseous tissue : secondary spongy state.

In ossifying or osteoplastic periostitis, there arise the so-called osteophytes from the periosteum, according to Billroth, from the surface of the bone by ossification of the granulating small vessels of the bone surface.

e. Exostosis is a tumor-like osseous new-formation, firmly attached to the bone.   There are distinguished, the circumscribed hyperostosis, exostosis in form of a spine or sharp crest, the rounded exostosis with compact surface and spongy centre ; enostosis, *i.e.*, exostosis in the interior of the bone.   Exostoses usually arise from the connective tissue of the periosteum or of the medullary (enostosis) ; more rarely from cartilaginous substance (so-called *exostosis cartilaginea*), especially from the peripheral layers of the epiphysal cartilage of the phalanges, represents a growth on the surface from the cartilage, thus a kind of articular extremity.

C. Osseous tumor, osteoma (or osteoid),

is a tumorous new-formation, in which ossification represents the regular, typical termination of development, while in many enchondromata, fibromata, etc., it is somewhat accidental.   Osteomata contain either almost only osseous tissue with vessels and periosteum : ost. durum s. eburneum ;

or there is besides in their interior a spongy bone-mass filled with medulla: OST. SPONGIOSUM ; or there are to be found large medullary cavities, which are by many times the largest portion of the tumor: OST. MEDULLOSUM S. MYELOIDES.

According to their locality, osteomata are HYPERPLASTIC or HETEROPLASTIC (in the brain, lungs. etc).

Osteomata. which proceed from connective or cartilage-tissue, are distinguished by the tissue from which they arise: most osteomata arise from CONNECTIVE TISSUE ; EXOSTOSIS CARTILAGINEA. which consists of compact or spongy bone tissue, and is covered with a thin layer of cartilage (especially in long tubular bones) ; HYPER-PLASTIC osteomata (COMMON EXOSTOSES), tendinous, aponeurotic, and apophytic osteomata. common and discontinuous osteomata, bony growths from riding or exercise, are mostly single, more rarely multiple (senile and infantile rheumatismus nodosus, syphilitic exostoses). HETEROPLASTIC osteomata pass partly into hyperplastic osteomata, especially the tendinous, etc. They lie in part near the bones (so-called parosteal osteomata). especially also in the vicinity of chronically inflamed joints, in the spinal and cerebral arachnoid, in the dura mater of the brain ; they lie in part separated from them : in the interior of the central nervous apparatus, within the eye, lungs. (Consult VIRCHOW, *Die krankh. Geschw.*, II., p. 1.)

An osteoma of the brain is described by EBSTEIN (*Virch. Arch.*, LI., p. 145).

BUHL calls diffuse osteomata of the lungs ossified knots in cirrhotic lungs (*Lungenentz*, etc., 1872, p. 61).

D. METAMORPHOSIS OF OTHER FORMS OF TISSUE INTO OSSEOUS TISSUE

occurs very often, but for the most part has little practical importance, since it either is of slight extent, or a consequent condition of other and more important processes, especially marasmus of age, chronic inflammations, and various new-formations.

A METAMORPHOSIS OF NORMAL CONNECTIVE TISSUE into osseous tissue often occurs with simultaneous calcification in tendons, fasciæ, intermuscular and interosseous ligaments ; in the vicinity of chronically inflamed joints ; in symphyses and synchondroses ; in the dura mater of the brain, especially the falx ; in the cerebral and spinal arachnoid ; in the brain itself ; in the valves of the heart and wall of the larger vessels, especially arteries ; in the skin, lungs, choroid, vitreous, atrophic eyes, etc.

On *myositis ossificans progressiva*, see MÜNCHMEYER (*Ztschr. f. rat. Med.*, 1868, XXXIV., p. 9).

A METAMORPHOSIS OF NEW-FORMED CONNECTIVE TISSUE into osseous tissue occurs : in pseudo-membranes of serous membranes, especially of the pleura, in new-formed connective tissue about chronically inflamed joints, in the hypertrophic interlobular connective tissue of the lungs, in cutaneous cicatrices, fibromata, enchondromata, carcinomata, cysts,—especially in tumors, which proceed from bones or periosteum, more rarely in those which have no connection therewith. In the latter case the osseous tissue is compact or porous, or both at the same time, for the most part small in proportion to the tumor, but sometimes very voluminous.

METAMORPHOSIS OF CARTILAGINOUS TISSUE into osseous tissue occurs : as an almost regular process of age, as well as after wounds and after chronic inflammations of the vicinity in the cartilages of the larynx, especially of the thyroid and cricoid cartilages, trachea, bronchi, ribs ; rarely in those of the joints, nose ; in cartilaginous tumors (as bony shell, or as cartilage-formation in the interior).

VII. NEW-FORMATION OF CARTILAGINOUS TISSUE.

J. MÜLLER, *Arch. d. Anat., Phys.,* etc., 1836. CCXX; *Geschwülste*, 1838, p. 31.—
HERZ, *De enchondromate,* Erlangen, 1843.—SCHAFFNER, *Ueb. d. Enchondrom.,*
Würzb., 1845.—RANKE, *De enchondromate,* Hal., 1848.—FICHTE, *Ueb. d. Enchon-*
drom., Tüb., 1850.—REDFERN, *Monthly J. of Med. Sc.,* X., p. 229, Sept., 1851.—
VIRCHOW, *Arch.,* 1853, V., p. 216; *Würzb. Verh.,* VII.; *Entwickelung des Schädel-*
grundes, 1857; *Die krkh. Geschw.,* 1863, I., p. 435.—SCHOLZ, *De enchondrom.,* Vra-
tisl, 1855.—O. WEBER, *Die Knochengeschw.,* 1856.—H. MECKEL, *Ann. d. Char.,* 1856,
VII., p. 60.—NEUMANN, *Arch. d. Heilk.,* 1870, XI., p. 414.

NEW-FORMED CARTILAGINOUS TISSUE has in general all the properties of the normal, fœtal, or developed cartilaginous tissue. It consists most frequently of hyaline, more rarely of reticular or fibrous cartilage. The basis substance is almost always chondrin, rarely containing gelatin or albumen.

According to NEUMANN (l. c.), liquid does not lie between the cartilage-cells and walls of the so-called cartilage-spaces, but a solid substance, which is in continuous connection with the remaining basis substance, and is to be regarded as a differentiated part of it: PERI-CELLULAR SUBSTANCE. Upon its origin depends the known wrinkling of the cartilage-cells: the latter are compressed in every increase of volume of the former.

According to HEITZMANN (*Wien. med. Jahrb.*, 1872, p. 349), the bodies of the cartilage-cells are provided with radiating processes, which form in the basis substance a delicate varicose net-work. At the points of transition of hyaline cartilage into striated fibrous cartilage and periosteal tissue the processes are very large and broad; they connect the neighboring cells immediately or mediately by means of fine processes.

Cartilaginous tissue ARISES either from cartilaginous tissue itself, or, and most frequently, from connective tissue, most rarely from osseous tissue. In the former case the cartilage-cells are divided, and secrete new basis substance. Or there appears, as in normal increase of thickness of cartilage, a metamorphosis of the lowest layers of the perichondrium in cartilaginous tissue. The same metamorphosis is met with sometimes in the connective tissue of other parts. In most cases, however, cartilaginous tissue arises from connective tissue by repeated division of the connective-tissue corpuscles, which become indifferent cells, and are then metamorphosed into cartilage-cells and secrete a basis substance. Its origin and GROWTH show nothing peculiar. The same holds good of most of its CHANGES.

New-formation of cartilaginous tissue occurs as regeneration of cartilage substance, most frequently in the intermediate state between hypertrophy and tumor, rarely as pure hypertrophy and as pure tumor.

A. REGENERATION OF CARTILAGINOUS TISSUE

takes place for the most part only slowly. It is observed most frequently in the costal cartilages, rarely in the joints. WOUNDS OF CARTILAGE heal for the most part only after many weeks, and almost always only by connective tissue. In lighter uncomplicated wounds there appears, with simultaneous softening of the cartilaginous basis substance, an increase of cartilage-cells at the cut surface; the new formed cells leave the cartilage capsules, come to the surface of the wound and form common connective tissue, and from which later cartilaginous tissue or osseous tissue may be produced.

In deeper or complicated wounds the same changes take place at a greater depth, and new vessels are formed from the vessels of the perichondrium.

DÖRNER (*De gravioribus quib. cartilaginum mutationibus*, Tüb., 1798) obtained the same results with respect to wounds of cartilage as were later arrived at by RED-FERN (l. c.).

According to REIZ (-STRICKER, *Ber. d. Wien. Acad.*, 1867, LV., p. 501), the surface of wounds of the trachea is filled by a fibrous cement-substance with nuclei, and the growing cartilage-cells send out filamentous processes, which reach from one wound-surface to the other.

According to ARCHANGELSKY (*Med. Ctrlbl.*, 1868, No. 42), the cicatrix of a cartilage-wound consists of connective tissue ; this after a time gradually passes into cartilage, whilst the connective-tissue corpuscles are transformed into cartilage corpuscles ; from this fibrous cartilage there is later formed the true or hyaline cartilage. BARTH (*Med. Ctrlbl.*, 1869, No. 40) observed regeneration in the costal cartilages of dogs and rabbits three months after their complete section ; union at first took place by new-formed connective tissue. LEGROS (*Gaz. méd. de Par.*, 1869, No. 66), as well as PEYRAUD (*Ibid.*, No. 28), experimentally found regeneration everywhere, when the perichondrium was retained. It proceeds from its lowest layer, *i.e.*, from the cells found in it.

THE SO-CALLED CARTILAGE CALLUS occurs sometimes in healing of fractures in man, and especially in many animals.

A COVERING OF NEW JOINTS WITH CARTILAGE is not infrequently observed after luxations, resections, in pseudarthroses.

B. HYPERTROPHY OF CARTILAGE

is rarely found pure, mostly in transitions into tumor.

UNIFORM THICKENING of cartilage, *e.g.*, of the bronchial cartilages, occurs in many bronchiectasiæ.

Outgrowth of cartilage, ECCHONDROSES, are represented by small, single, or multiple tumors, which occur not infrequently on the ribs, in the larynx and trachea, in articular cartilages, especially of the symphysis pubis, in *arthritis deformans*, also in the periphery of joints, and are mostly of no practical importance. (The so-called *ecchondrosis spheno-occipitalis* is a remains of the fœtal chorda dorsalis.)

DENDRITIC VEGETATION forms small or larger, tufted formations, which are composed chiefly of vascular connective tissue on the free portion of cartilage-substance. They arise from synovial membranes, or from the periosteum, or from articular cartilage, especially of the knee-joint. The cartilaginous masses of the surfaces of joints, pediculated, mostly small, rarely reaching the size of a walnut, may finally, sometimes after succeeding partial calcification or ossification, become free : so-called FREE BODIES IN THE JOINTS.

C. CARTILAGINOUS TUMOR, ENCHONDROMA OR CHONDROMA.

Enchondroma is a single or multiple, mostly circumscribed, rounded tumor of varying size, with smooth or glandulous or lobed surface. Enchondromata consist almost never of cartilaginous substance alone, and indeed of one or many kinds of it, but at the same time almost always also of vascular connective tissue.

Consequently, enchondromata on cut surfaces vary greatly in color, consistence, etc. First, with respect to the KIND OF CARTILAGE, they consist either (and most often) of hyaline cartilage ; or (more rarely and only with other kinds of cartilage) of reticular cartilage ; or of fibrous cartilage with homogeneous or fibrous basis substance—so-called HARD ENCHONDROMATA ;

or of mucous cartilage, *i.e.*, of a mucous basis substance with round, oval, stellate, etc., cartilage-cells deposited therein—so-called SOFT or GELATINOUS ENCHONDROMATA. These kinds of cartilage sometimes form of themselves alone the whole tumor, sometimes they occur together in the same tumor, and are then sharply contrasted, or pass gradually into one another. Also with respect to the KIND, QUANTITY, and DISTRIBUTION of the CONNECTIVE TISSUE occurring at the same time, and varying in VASCULARITY: the quantity of it varies so greatly, that many enchondromata appear to the naked eye as connective-tissue tumors, in which there is no cartilage, or only scanty islands of cartilage. It forms always the capsule and often the sheath-wall of vessels in the interior.

SOFT or GELATINOUS ENCHONDROMA (*ench. molle s. gelatinosum*) contains essentially larger stellate cells, is very moist, and shows a peculiar slippery, cut-surface like albumen of eggs. If it is rich in mucus, there is formed the ENCH. MUCOSUM, which must be distinguished from the secondary softening of other enchondromata. If it contains stellate cells, there arises MECKEL'S stellate corpuscle-tumor, VIRCHOW'S *ench. myxomatodes* if the cartilage, VIRCHOW'S *myxoma cartilagineum* if the mucous tissue preponderates. Soft enchondromata contain an albuminous basis substance, thus arises VIRCHOW'S ENCH. ALBUMINOSUM.

The MICROSCOPICAL INVESTIGATION of enchondromata furnishes manifold departures from the structure of the normal, embryonic, and formed types of cartilage. The quantity of cartilage-cells is for the most part very variable, as in normal cartilage; sometimes very small, sometimes so large that the cells are flattened on opposite sides. Likewise with this arrangement, the size and form are manifold: the cells are often spindle-shaped or stellate and movable, whereby these tumors resemble mucous tissue, so much the more, as the basis substance is at the same time soft, even almost liquid. The membrane of cartilage-cells is sometimes double as in normal cartilage, sometimes it consists of many concentric layers, sometimes it is simple (osteoid enchondroma), sometimes every membrane seems to be wanting, so that free nuclei appear to be deposited in the basis substance. Fat-drops are for the most part found in the cell-contents. The cell-nucleus is single, multiple, of varying size, form (sometimes branched) and often in fatty metamorphosis or simple atrophy. The basis substance is of varying thickness and character.

Further and more numerous differences arise through metamorphoses, which frequently occur in all the tissues of enchondroma. Aside from those, which also are shown by normal cartilage in greater or less degree (fatty infiltration and calcification of the cells) clouding and fibrous change of the intercellular substance), the following are especially worthy of mention:

VASCULARIZATION, which in many enchondromata precedes ossification, in others reaches a teleangiectatic development;

CALCIFICATION, which affects only the cells, or only the basis substance, or both at the same time;

OSSIFICATION, which occurs as well in enchondromata of soft parts, as especially in those of bones, and affects sometimes only single, central or peripheral parts of the tumor, sometimes the latter in their whole extent, so that the tumor finally becomes an osteoid, sometimes the whole periphery of the tumor, so that the latter is inclosed by a bony shell, sometimes only a half of the enchondroma (*e.g.*, in those of the periosteum the parts on the side of the latter);

TUBERCULIZATION, which depends upon a for the most part partial metamorphosis of the enchondroma into a substance like yellow tubercle; and

SOFTENING, which consists in a fatty metamorphosis of the cells and in a mucous metamorphosis of the basis substance. It appears in few or very numerous points, or in the whole mass of the tumor, especially of large and soft enchondromata of bones. The affected parts are soft like jelly, honey or synovia, clear or clouded, pale yellow-

ish or reddish in color; sometimes they inclose small cartilaginous remains. The internal surface of the cavities is for the most part uneven through normal or incompletely softened cartilage masses, rarely it is smooth. In the latter case there arises the so-called CYSTIC or CYSTOID ENCHONDROMA. Sometimes the cavities break through outwardly: common or fistulous enchondromatous ulcer.

Enchondromata occur especially in young individuals, sometimes even in the new-born. They oftenest affect the bones, more frequently their centre, especially in the bones of the hand of children, than their periphery and the periosteum, especially in adults (besides the bones of the hand and foot, especially the femur, tibia, humerus, pelvic bones, ribs, upper maxilla). Therein the articular surfaces almost always remain unaffected, even if, as not infrequently happens, the upper and lower bones of the joint are enchondromatous (e.g., in the bones of the hand and foot, in the knee-joint); also the surrounding soft parts remain for the most part intact. Enchondromata are more rarely found in the connective tissue of the skin, and between muscles, tendons, ligaments, intestines, on fasciæ, in the vicinity of and within glandular organs (most frequently in the testicles, parotid and submaxillary glands, lungs, mammæ, ovaries—in all these parts for the most part combined with other tissues), in the brain, uterus, etc. Enchondromata are found most rarely in cartilage itself: e.g., in the septum narium.

With respect to the ORIGIN of enchondromata, there remain, according to VIRCHOW, sometimes in growing bones some fragments of the original cartilage unossified, which later become the points of departure for the formation of tumor, e.g., in rachitis. Agreeing with this is the knowledge of the fact, that enchondromata often occur in parts of bone, which normally ossify late and irregularly, e.g., in the vicinity of the synchondroses spheno-occipitalis, ilio-pubica, sacro-iliaca, in the vicinity of the epiphysal cartilages of tubular bones. Also enchondromata are not infrequently found in retained testicles, after traumatic influences, at points of fracture.

The GROWTH of enchondromata takes place for the most part concentrically, rarely so, that around the mother-tumors are formed new or daughter-tumors. Enchondromata grow for the most part slowly, sometimes to a considerable size, but then they may remain stationary; rarely they enlarge quickly (many enchondromata of the testicles and parotid glands).

Enchondromata occur for the most part single; more rarely several are formed, or even many at the same time or soon after one another: especially in the phalanges of the fingers and toes of children, in the lungs.

Enchondromata INJURE the affected organ and the whole organism for the most part only by their seat and size; more rarely also by softening and ichorous formation. The simultaneous occurrence of numerous enchondromata is sometimes followed in children by a cachexia. Healing usually follows complete extirpation. In rare cases, especially in soft enchondromata, like tumors are developed in the appertaining lymph- and blood-vessels, in the lymph-glands, in internal organs, especially the lungs. Further extension takes place through embolism.

Consult the exquisite cases by O. WEBER (*Virch. Arch.*, XXXV., p. 501), and by BIRCH-HIRSCHFELD (*Arch. d. Heilk.*, X., p. 468).

Enchondromata not infrequently occur COMBINED with other tissues and tumors, most frequently with connective tissue, mucous tissue, fatty tissue, sarcoma, adenoma (salivary glands), carcinoma (testicle), cysts (ovaries).

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OSTEOID ENCHONDROMA (VIRCHOW) furnishes by boiling not chondrin, but gelatin; its cells are not encapsuled, but lie free in the intercellular substance; they are for the most part small, rarely round, mostly elongated, spindle-shaped or lenticular, sometimes provided with processes; the very abundant vascular intercellular substance is not fibrillar, but forms dense laminæ, trabeculæ or net-works, between which the cells are often scarcely recognized: in this there arises a great similarity with many fibromata. Osteoid enchondromata form in part the largest (in the circumference) of the tumors of bone. They surround for the most part the whole bone. They are most frequent at the knee-joint—extremities of the femur and tibia. They have for the most part no bony shell. They contain sometimes only a small amount of calcareous salts and can be cut, but sometimes can only be sawn, especially at the base. Their uniform termination is ossification, rarely softening. Metastases also occur into internal organs.

VIII. NEW-FORMATION OF MUSCULAR TISSUE.

J. VOGEL, *Icon. hist. pathol.*, 1843, Taf.. IV.—O. WEBER. *Virch. Arch.*, 1854, VII., p. 115; *Med. Centralbl.*, 1863, No. 34; *Virch. Arch.*, XXXIX., p. 216.—BILLROTH, *Virch. Arch.*, 1855, VIII., p. 433; IX., p. 172.—WITTICH, *Königsb. Jb.*, 1861, III., p. 49.—DEITERS, *Arch. f. Anat. Phys.*, u. s. w., 1861, p. 393.—PEREMESCHKO, *Virch. Arch.*, 1863, XXVII., p. 116.—COLBERG, *Deutsche Klin.*, 1864, No. 19.—ZENKER, *Ueb. d. Veränd. d. willk. Muskeln im Typh. abd.*, 1864, p. 51.—BUHL, *Ztschr. f. Biol.*, 1865, I., p. 263.—VIRCHOW, *Die krkh. Geschw.*, 1867, III.. 1. H., p. 96.—NEUMANN, *Arch. f. micr. Anat.*, 1868, IV., p. 323; *Arch. d. Heilk.*, 1868, IX., p. 364.—HOFFMANN, *Virch. Arch.*, XL., p. 505.

NEW-FORMATION OF MUSCULAR SUBSTANCE occurs as regeneration, as hypertrophy, and as tumor, as well in transversely striated as in smooth muscular fibres, and indeed most of these forms are of frequent occurrence.

1. NEW-FORMATION OF TRANSVERSELY STRIATED MUSCULAR FIBRES.

A. REGENERATION OF TRANSVERSELY STRIATED MUSCULAR FIBRES is found either AFTER DEGENERATIVE LOSSES OF SUBSTANCE, *i.e.*, after those, where the primitive bundles degenerate, are destroyed and finally disappear, while the muscular stroma and bloodvessels remain unaffected; or, AFTER DESTRUCTIVE LOSSES OF SUBSTANCE, *i.e.*, after those, where in consequence of cutting, laceration (about fractures of bones, etc.), of wounds with loss of substance, by suppuration, etc., all parts of the muscle (muscular fibres, stroma, vessels and nerves) are destroyed. Regeneration, according to some, proceeds from the perimysium, from the sarcolemma, and especially from the muscular corpuscles, perhaps also from the nuclei of the capillaries, etc., in a manner probably similar to the physiological formation of muscle; according to others, it takes place by longitudinal splitting, etc., of the old muscular fibres.

The theories of the origin of new-formed muscular fibres widely differ. According to most (PEREMESCHKO, COLBERG, BUHL, HOFFMANN) the so-called muscular corpuscles are especially concerned; according to others (WITTICH, DEITERS, ZENKER, WALDEYER and others), new muscular fibres proceed from connective tissue. See also GUSSENBAUER (*Arch. f. klin. Chir.*, 1871, XII., p. 1010).

According to BUHL, REMAK and others, pathological (as well as normal) muscle is enlarged always by a preceding division of the muscular nuclei in the transverse and in the long axis of the primitive bundle: thence is derived the elongation and increase in number of the bundles. By the longitudinal division of the nuclei there arise divisions and splittings of the bundles in the direction of their length. Also, according to NEUMANN, regeneration of degenerated muscles takes place in typhoid fever by a longitudinal splitting of old fibres. The sarcolemma is found in the inter-

cellular substance of the perimysium. In this the nuclei of the muscular fibres take no part.

According to NEUMANN, the healing process of muscular wounds, like their regeneration in typhoid fever, consists in a gradual growth of the cut muscular fibres into the cicatricial tissue and through it, so that finally the separated ends of the fibres on both sides meet.

According to MASLOWSKY (*Wien. Wochenschr.*, 1868, No. 12) transversely striated muscular fibres are regenerated for the greatest part from migrated colorless blood-corpuscles. Similar to this view is that of AUFRECHT (*Virch. Arch.*, XLIV., p. 180). Both, as well as KREMIANSKY (l. c.), support their statements chiefly on the fact, that they have also found by injection of cinnabar into the vessels, some spindle-shaped cells of the cicatricial tissue containing cinnabar. According to MASL., the old muscular tissue contributes nothing to formation of the new. According to AUFRECHT, this is the case and the muscular bundle is regenerated within the sarcolemma, if the latter is retained in the wound.

WEBER, by experimental investigation, found young muscular cells already on the second day after injury; from the beginning the second week these were very long, small and like primitive bundles. After four weeks, young muscles were perfectly developed.

a. THE RESTORATIVE REGENERATION OF MUSCLES, which appears after degenerative losses of substance, occurs almost regularly in all severe febrile diseases, especially in typhus and typhoid fevers (in muscular fibres destroyed by granular, waxy or fatty degeneration—see p. 331), and in trichinosis (see p. 126), not infrequently in progressive muscular atrophy, and so-called essential paralysis of children, in traumatic and lead paralyses.

WITTICH first demonstrated the PHYSIOLOGICAL regeneration of transversely striated muscles; while in frogs, in the sleep of winter, the older muscular bundles waste by fatty metamorphosis, there appears a very extensive regeneration. WEISSMANN (*Ztschr. f. rat. Med.*, C. X., p. 279) saw the same in a frog, which by scanty nourishment had emaciated in the water to a skeleton, when in May and June it had received abundant food. KÖLLIKER, *Hdb. d. Gewebel.*, 1862, p. 214. COLBERG, ZENKER. Clinical observations of DUCHENNE of Boulogne: *de l'electrisation localisée*, 1855, 2. Ed. *De la paralysie musculaire pseudo-hypertrophique ou paralysie myosclérosique*, Paris, 1868.

b. RECONSTRUCTIVE MUSCULAR REGENERATION, which serves for filling up after destructive losses of substance, appears only occasionally, whilst in most cases there is formed a vascular connective-tissue cicatrix.

(DEITERS, PEREMESCHKO, WEBER.)

B. HYPERTROPHY OF TRANSVERSELY STRIATED MUSCULAR FIBRES

is often found in the muscles of the trunk and extremities, as well as in the heart. In the muscles of the trunk and extremities muscular hypertrophy is for the most part a result of increased activity (laborers, gymnasts, dancers, etc.); in the respiratory muscles (including the diaphragm) it appears in consequence of labored respiratory movements, especially during emphysema; in the heart it occurs on both sides or only in one half, in the ventricle as well as in the auricle, in consequence of increased activity as so-called concentric, simple, and excentric hypertrophy. In rare cases and from unknown causes the latter hypertrophy affects the tongue. In the latter part it forms a severe affection, making operation necessary. In the heart and respiratory muscles it is of the greatest practical importance, since it affects a so-called COMPENSATION of the underlying affections of the lungs, heart, great vessels, kidneys. The utility of this compensation ceases as soon as the new-formed muscular fibres degenerate or disappear.

MICROSCOPICALLY, muscular hypertrophy consists in a thickening of pre-

existing primitive bundles and in a new-formation of these. The especial relations are not yet accurately known.

VOGEL.—BARDELEBEN, *Virch. Arch.*, I., p. 487.—LEBERT, *Traité d'anat. path.*, I., p. 448.—FÖRSTER, *Hdb.*, p. 804 ; *Spec. path. Anat.*, 2. Aufl., 1863, p. 659.— HESCHL, l. c., p. 71.—BUDGE, *Arch. f. phys. Heilk.*, 1858, p. 71.—MARGO, *Neue Unters. üb. d. Entw. d. Muskelf.*, 1861.—FRIEDREICH, *Krkh. d. Herzens.*, 1861, p. 286.—O. WEBER.)

AUERBACH (*Virch. Arch.*, 1871, LIII., p. 234 et 397) has observed a case of TRUE MUSCULAR HYPERTROPHY, in which the elements of the right biceps exceeded in breadth those of the left by one-half. In the hypertrophic muscles there were found at the same time a very important nuclear growth, which was almost proportionate to the increase in volume. The muscles as well as overlying skin were richer in blood-supply. COHNHEIM and EULENBERG found in muscular hypertrophy the muscular cylinders for the greatest part atrophic, but besides, some of colossal breadth. (See p. 306.)

According to MAAS (*Arch. f. klin. Chir.*, 1872, XIII., p. 413) in MACROGLOSSIA there is originally a hyperplasia of the whole or half of the tongue ; the enlarged tongue, not having room in the mouth, is exposed to manifold external irritants, is attacked by inflammations, the product of which is new-formation of vessels and connective tissue.

According to SCHIFF (*Wien. med. Jahrb.*, 1872, p. 247) the *ligamentum uteri rotundum* shows on its upper border three portions of transversely striated muscular fibres, which, after they have reached the internal inguinal ring, are reflected to the transverse muscle of the abdomen. In the puerperal state they are considerably increased. They are according to HENLE analogous to the two cremasters of man.

C. TUMOR OF TRANSVERSELY STRIATED MUSCULAR FIBRES

(RHABDOMYOMA, *myoma striocellulare*, myosarcoma, true myoma)

rarely occurs PURE (heart, tongue, body, extremities, testicles), for the most part MIXED in form—tumors of the testicles and of the ovaries (commonly cystoid) containing numerous other tissues, also of the perineal region, mediastinum, perhaps also of the brain, rarely in other tumors (keloid, cancer).

Observations of ROKITANSKY, VIRCHOW, O. WEBER, BILLROTH, BENJAMIN, SENFTLEBEN, WALLMANN, RECKLINGHAUSEN, LAMBL, BUHL, and the author. According to BUHL, who denies the new-formation of specific tissue-elements in adults, transversely striated muscles have been found in the embryo abnormally in the testicles or ovaries, etc.

2. NEW-FORMATION OF SMOOTH MUSCULAR FIBRES.

This occurs in the form of hypertrophy and tumor; its regeneration is not yet known.

Sometimes textures more or less like smooth muscular fibres occur also with other tissues, *e.g.*, in enchondromata, sarcomata, cancers. We do not however yet know any safe rule by which to recognize them.

A. HYPERTROPHY OF SMOOTH MUSCULAR FIBRES

consists in a great increase of them, especially of their number. It is not infrequently found in the stomach, intestines, œsophagus, uterus, urinary bladder, prostate gland, bloodvessels, from various CAUSES, generally in consequence of INCREASED ACTIVITY of these organs. The latter depends upon irritations of various kinds, especially inflammations, as well as in strictures between the hypertrophic organ and the surface affected (stenosis

of the œsophagus, pylorus, urethra, etc.). In the latter case the hyper-trophy serves as compensation of the stricture or stenosis often, so perfectly that the injurious effect of the stricture appears only when the hypertrophy from any cause disappears (most frequently by fatty metamorphosis). Hypertrophy affects, in membranous organs, almost always the intermediate connective tissue, as well as the connective tissue of the serous, subserous, mucous and submucous tissue, in the prostate often simultaneously also with the glandular tissue.

MICROSCOPICALLY, new-formed muscular fibres usually perfectly resemble the normal fibres; therewith are also commonly found some of remarkable length and breadth. Hypertrophy probably occurs by division of muscular fibres already present.

An enlargement and new-formation of organic muscular fibres occurs PHYSIOLOG-ICALLY in the female genitals as consequences of conception. The uterus, at the end of pregnancy, shows nearly a twenty-four fold increase in size, which is chiefly dependent upon muscular tissue. The muscular fibres are considerably enlarged (to form three to eleven times their length, and from two to five times their breadth), and to the sixth month there is a new-formation of numerous muscular fibres; also the intermuscular connective tissue, etc., increases (KÖLLIKER). The round liga-ments, as well as the muscular bundles radiating from the most external layer of transverse fibres of the uterus between the two laminæ of the broad ligament, like-wise increase considerably in size during pregnancy and acquire an excessive strength. LUSCHKA found the same, especially in cases in which the broad liga-ments had continually experienced a considerable tension, especially in prolapsus uteri of long standing, developed in a superior degree (*Müll. Arch.*, 1862, p. 204). At the time of heat, or of menstruation the spindle-shaped cells of the stroma of the ovaries (according to ROUGET, AEBY and others, the muscular fibres) are more strongly developed (AEBY, *Reich. u. Dub.'s Arch.*, 1861, p. 635). Also at the time of pregnancy they are much more developed (GROHE, KLEBS).

Smooth muscular fibres, according to KÖLLIKER (*Z. f. wiss. Zool.*, I., p. 72), FÖRSTER, *Hdb.*, p. 260), ARNOLD, and others, are formed from connective tissue, according to MOLESCHOTT and PISO-BORME (*Unters. z. Naturl.*, IX., p. 5) from muscular fibres themselves, partly by longitudinal splitting, partly by branching and budding.

JOHNSON (*Royol Med. and Chir. Soc.*, Dec., 1867) found the muscular layer of the small renal arteries very hypertrophic in all forms of chronic Bright's disease.

A strong enlargement of smooth muscular fibres is found also in ectatic veins, those with thick as well as those with thin walls (SOBOROFF, *Virch. Arch.*, 1872, LIV., p. 306).

In many cases of chronic interstitial pneumonia (CORRIGAN'S cirrhosis of the lungs) there is found in the walls of the alveoli a new-formation not only of con-nective tissue, but also or even chiefly of smooth muscular fibres (BUHL's muscular cirrhosis, in opposition to the fibrous. See *Lungenentz*, etc., p. 58).

According to EBERTH (*Med. Ctrlbl.*, 1872, No. 15), there occurs on the surface of the human kidney a wide meshed net-work of smooth muscular fibres. In the stroma of the kidney itself, as well as in the capsule it is wanting, and yet small processes extend into the most superficial layers of the cortical substance.

NEW-FORMATION OF SMOOTH MUSCULAR FIBRES INDEPENDENTLY OF PRE-EXIST-ING SMOOTH MUSCULAR FIBRES, as in many membranes, in many sarcomata, etc., has not yet been certainly demonstrated. ARNOLD (*Virch. Arch.*, XXXIX., p. 270) found in a case of old empyema on the inner surface of the sack such quantities of smooth new-formed muscular fibres, that they formed a continuous tolerably thick muscular covering; they arose from rounded cells, most of which were situated toward the interior. A case earlier observed in the pleura and pericardium by LEO-WOLF (*Heidelb. Diss.*, 1832) presented an entirely similar character. NEUMANN (*Arch. d. Heilk.*, X., p. 600) has shown on the other hand, that the characters of the above cases are not sufficient for the cells in question to be regarded as smooth muscular fibres, that these are much more probably connected with the development of new connective tissue.

B. Tumor of smooth muscular fibres

(MYOMA, LEIOMYOMA, FIBROMYOMA, FIBROID in the narrower sense, myo-fibroid)

is in general like common fibroma (p. 385), of varying size, round, for the most part sharply circumscribed and easily enucleated. Its cut surface is smooth or uneven, glistening and similar, with respect to its contained smooth muscular fibres, to fibroma; or grayish-red, soft, irregularly fibrous; or consisting of small, diffuse, firmly connected, rounded tumors; or showing concentric laminæ.

The MICROSCOPE shows besides common connective tissue and vessels, organic muscular fibres in varying quantities, rarely so that these form only the smallest portion of the tumor, but usually constitute its chief element. The muscular fibres lie sometimes imbedded in a for the most part scanty, rarely abundant connective tissue; sometimes they form perfect trabeculæ of varying strength.

Myoma occurs by far most frequently in the body of the uterus, alone or in numbers, and in its immediate vicinity: it lies in its muscular substance (so-called interstitial myoma), or under the serous tunic, the latter sometimes with a pedicle (so-called subserous myoma), or under the mucous membranes (so-called polypous myoma or fibrous polyp). It is more rarely found in the stomach, intestines, œsophagus, in the prostate (for the most part as so-called hypertrophy of the middle lobe), in the skin especially in the scrotum, in the walls of the veins (v. saphena and ulnaris).

The METAMORPHOSES and COMBINATIONS, as well as the CONSEQUENCES of myoma are the same as those of fibroma. Especially worthy of note is the MYOMA CAVERNOSUM s. teleangiectodes, which not infrequently has the capacity of acute swelling and subsidence.

The CAUSES of myoma are: advanced age, great use, catarrhs of the affected mucous membrane.

IX. NEW-FORMATION OF NERVOUS TISSUE.

ARNEMANN, *Vers.*, *üb. Gehirn. u. Rückenmark.* 1787.—FLOURENS, *Ann.*, *d. sc nat.*, 1828, XXXIII.—STEINRÜCK, *De nerv. regenerat.*, 1838.—NASSE. *Müll. Arch.*, 1839, p. 405.—SCHÖN, *Müll. Arch.*, 1840.—LANGER. *Bau d. Nerven*, 1842.—BROWN-SÉQUARD, *Gaz. méd.* de Par., March, 1850.—WALLER, *Müll. Arch.*, 1852, p. 392. —BRUCH, *Ztschr. für wissenschaftl. Zool.*, 1854, VI., p. 135.—WEDL, *Ztschr. d. Wien. Aerzte*, 1855, XI., p. 13.—LENT, *De nervorum dissectorum commutat. ac regenerat.*, *Berol.*, 1855.—FÜHRER, *Arch. f. phys. Heilk.*, 1856, p. 248.—MARFELS, *Corr.-Bl. d. d. Ges. f. Psych.*, 1857.—KLOB, *Ztschr. d. Wien. Aerzte*, 1858.—BUHL, *Aerztl. bayerisches Intelligenzbl.*, 1858.—GLUGE ET THIERNESSE, *Bull. de l'acad. r. d. sc.* à Brux., 1859.—PHILIPPEAUX et VULPIAN, *Gaz. méd.*, 1860, Nos. 27–39.— HJELT, *Virch. Arch.*, 1860, XIX., p. 352.—REMAK, *Virch. Arch.*, 1862, XXIII., p. 441.—SCHIFF, *Arch. d. Ver. f. gemeinschaftl.*, Arb. I., p. 700]; II., p. 413.—NEU-MANN, *Arch. d. Heilk.*, IX., p. 193.—VIRCHOW, *Würzb. Verh.*, I., p. 141; *Arch.*, III., p. 256; *D. krankh. Geschw.*, III., 1. H., p. 233.—HERTZ. *Virch. Arch.*, 1869, XLVI., p. 251.—ERB, *D. Arch., f. klin. Med.*, 1869, V., p. 42.—BENECKE, *Virch. Arch.*, LV., p. 496.

NEW-FORMATION OF NERVE-TISSUE occurs almost always in the form of nerve-fibres, very rarely in that of ganglion-cells. In the former it is found as regeneration, as hypertrophy, and as nerve-tumor.

According to RANVIER (*Compt. rend.*, LXXIII., 1871, II., p. 1168) every small nerve lies in a serous or lymphatic hollow space. A layer of endothelial cells with the connective tissue surrounding it, is to be regarded as its parietal layer. The visceral

layer corresponds to the external surface of the sheath of Schwann, and consists probably of flat cells. The nutritive fluids circulate in this hollow space and reach the axis-cylinder through a colloid substance, which form peculiar constricting rings. Consult also A. KEY and RETZIUS, *Arch. f. micr. Anat.*, 1873, IX., p. 308. The PERINEURIUM OF ROBIN is the envelope around each nerve-bundle, the ENDONEURIUM is the connective tissue in the nerve-bundle itself, the EPINEURIUM is the connecting connective tissue outside of the perineurium between the bundles. According to RANVIER (*Arch. de physiol. norm. et path.*, 1872, IV., p. 129), nerve-fibres show ring-shaped constrictions, in which the medullary sheath is wanting. The portion of a primitive fibre lying between two constrictions always possesses only one nucleus, which lies almost exactly at a middle point between two constrictions.

A. THE REGENERATION OF DIVIDED NERVES

is effected differently, according as the previous division was simple or at the same time with resection of a piece of the nerve. In both cases the portion of the nerve above the point of division remains NORMAL (influence of the nervous central organ), while the nerve-fibres below the point of division (according to many only immediately below this, according to others in their whole course to their terminal distribution) degenerate. DEGENERATION leaves the sheaths of the fibres intact, AFFECTING ESPECIALLY THE MEDULLA, in less degree the axis-cylinder. It consists at first in a slight coagulation of the medulla; then in an indentation and breaking up into numerous small pieces, which are at first angular, later rounded; finally in a fatty metamorphosis of the latter with final resorption. According to many the axis-cylinder (which probably conducts nerve irritations) remains normal, according to others it is destroyed. According to many, in consequence of the metamorphosis of the medulla, the differentiation between medulla and axis-cylinder ceases and the degeneration of the fibres consists in a return to the embryonic state, where this distinction likewise does not exist. In the sheath of the fibres numerous nuclei appear, in the interior serum collects.

After SIMPLE DIVISION of the nerves there appears an immediate union of the cellular sheath and axis-cylinder, destruction of the medulla and perhaps also of the axis-cylinder of the nerve-fibres of the peripheral end and subsequent regeneration of it. After RESECTION OF A PIECE OF NERVE there follows a degeneration of the fibres of the peripheral end of the nerve. The latter, as well as regeneration of these and that of the resected piece of nerve is differently described by different authors: according to most, the nuclei of the neurilemma undergo repeated division and then secrete a homogeneous mass, later becoming nerve-substance. The length of the resected piece, which is regenerated, may extend to 2–8 even 12–20 mm.

According to a more recent view, no essential difference exists in the regeneration, whether the nerve is simply divided or a piece is resected. New nerve-fibres arise in the central end of the nerve by an endogenous formation of daughter-fibres within the old fibres; in the peripheral end new fibres are formed within the degenerated old fibres. Reunion of the new fibres arising in the peripheral portion of the nerve with the same fibres of the central portion follows probably from the ingrowing of the fibres of both ends of the nerve into the granulation-tissue.

Very different theories exist, respecting the HISTOLOGICAL RELATIONS OF NERVE-REGENERATION AFTER DIVISIONS. BRUCH and SCHIFF saw sometimes an immediate union of the extremities of nerves without previous degeneration, a so-called *reunio per primam intentionem*. HERTZ found a similar thing.

According to WALLER and BRUCH, all the primitive fibrillæ of the peripheral portion of the nerve are completely destroyed, and that complete regeneration proceeds from the central portion. According to LENT, of the primitive fibrillæ in the peri-

pheral portion only the axis cylinder and medulla degenerate, which are again formed from the remaining cellular sheath. According to SCHIFF, only the medulla degenerates in the peripheral portion of nerves; the spaces are filled with new primitive fibrillæ, which grow from both ends and are here united; then appear pale cylindrical striæ, in which are formed at first the axis-cylinder, then the cellular sheath, finally the medulla. According to LENT, HJELT and others, the number of nuclei in the connective-tissue sheaths increases remarkably after division of a nerve, as well in the cicatrix as in the peripheral piece, and the new nerve-fibres probably arise from them.

LAVERAN (*Journ. de l'anat. et de la phys.*, 1868, p. 305), and especially HERTZ, regard the round, as well as the spindle-shaped cells proceeding from them, which lie in the sheath, between the fibres of the peripheral portion of the nerve and in the central swelling, as migrated colorless blood-corpuscles or their descendants.

REMAK concludes from an experiment, in which he examined the sciatic nerve eight months after division, that new nerve-fibres are formed within the sheath of Schwann, and indeed in place of one fibre many fibres were formed, that they probably arise from the axis-cylinder and by longitudinal division of it. According to NEUMANN, the fibres of the central end of the nerve suffer a degeneration and a regeneration. The former consists in the disappearance of the medulla to the same extent, in which granulation-tissue is formed in the cellular sheath. Regeneration consists at first in an increase in breadth of the fibres, which especially affects the primitive sheath; then in a longitudinal striation of the fibres and in a final splitting of the ends of the fibres into bundles of pale small parallel ribbons which extend above into medullated fibres, below into granulation tissue. Contrary to REMAK, N. finds not only the axis-cylinder, but this and the metamorphosed medulla to split longitudinally. Gradually the fibres from the centre to the periphery become medullated: either by deposit of medulla, or by metamorphosis of their external layer. Finally, the thickened primitive sheath of the mother-fibres probably grows in between the individual daughter-fibres. Regeneration of the peripheral end of nerves results in like manner, and independently of the central end.

According to RANVIER (*Compt. rend.*, 1872, LXXV., p. 1831) the nuclei of the sheath of Schwann in the PERIPHERAL ends of nerves between two ring-shaped constrictions are, twenty-four hours after division of the sciatic or vagus, slightly swollen, surrounded with granular protoplasm. Forty-eight hours after, the nucleus is still larger, the protoplasm so swollen, that it penetrates the medullary sheath. After seventy-two hours, the nucleus is so large, that it fills almost the whole diameter of the primitive fibres; the medullary sheath is interrupted by a protoplasmic mass filled with fat; the axis-cylinder is likewise interrupted. On the sixth day, the medullary sheath consists of small well-defined particles; the protoplasm contains numerous fat-granules, the nuclei of Schwann are increased. Fat-granules are found in the flat cells of the intra-fascicular connective tissue, and in the endothelium of the bloodvessels of the sheath. From the seventh to the twentieth day the nuclei no longer increase, the protoplasm is more scanty, the fractured portions of the medullary sheath are here and there spindle-shaped. In the CENTRAL portion of the nerve, myelin is distributed in fine fat-drops; the axis-cylinder is retained; the nuclei likewise increase and lie flattened between axis-cylinder and sheath of Schwann. According to RANVIER's (*Gaz. d. hôp.*, 1873, No. 26) experiments on the vagus, new-formation of divided nerves proceeds from the central ends. The nerve-bundles then arising form at first a filament, which extends toward the peripheral end, then is united with the degenerated fibres themselves.

PHILIPPEAUX and VULPIAN (*Gaz. des. hôp.*, 1861, No. 52) saw portions of nerves, separated from the centre, regenerated, when no reunion resulted with the central portions. They resected a piece, almost 25 mm. long, from the lingual nerve in two dogs and transplanted it under the skin in the inguinal region. After six months they found not only in the peripheral, isolated remaining piece of the lingual nerve very numerous new-formed nerve-fibres, but also in the transplanted piece a number of fine fibres of the thickness for the most part of 0.005 mm.

After division of nerves, the pale terminal fibres in the interior of the motor terminal plate degenerate, while its nuclei and finely granular substance remain unchanged (KRAUSE. *Ztschr. f. rat. Med.*, 1863, XXI., p. 73). Concerning the regeneration of the finest nerve-fibres, nerve terminal plates, etc., we know nothing.

BIDDER (*Arch. f. Anat., Phys.*, etc., 1865, p. 67) found after division of the anterior and posterior roots of the nerves going to the posterior extremities, fatty degeneration of the nerves of the anterior root, but on the other hand, a normal condition of the nerves of the posterior roots, as well as of the sympathetic nerves.

(The nerve-fibres in the spinal cord are similarly affected in injuries and diseases of the cord.)

COURVOISIER (*Arch. f. micr. Anat.*, II., 1, H., p. 13) has made use of the changes of the central and peripheric portions after section, to determine the direction of the course of the nerve fibres of the communicating branches of the sympathetic. Herein he observed in the (from the proper ganglion-cell) peripheral nerve-fibres at first coagulation of the medulla, then resorption of fat-globules and of the axis-cylinder, until finally the connective tissue sheath of the fibre is emptied and collapses. The nerve-cells also succumb to fatty degeneration.

After BRUISING OF NERVES the medulla of the nerve-fibres undergoes the same changes as after division; but ERB could demonstrate histologically as well as physiologically, that thereafter the axis-cylinder persisted in the peripheric portion. ERB likewise found at the point of bruise a considerable thickening of the neurilemma, caused at first by round, then by spindle-shaped cells, which thickening prevents regeneration of the nerves, but probably later disappears.

[Consult VULPIAN, *Arch. de Phys.*, 1874, p. 704.—COSSY ET DEJERINE, *Arch. de Phys.*, 1875, p. 567.—S. WEIR MITCHELL, *Injuries of Nerves*, Phila., 1872.—ED.]

The DURATION OF NERVE REGENERATION is shortest after simple incised wounds, as has been shown by surgical practice and experimental research. It is longer after resection of a piece of a nerve. If the latter exceeds a certain length (2–4 cent.) regeneration will not take place. In general, sensory nerves re-unite with restoration of function more easily than motor nerves. After healing of incised wounds of mixed nerves, sensibility is restored earlier than motility.

DESCOT observed healing and complete restoration of function of divided nerves, in 40 days, SCHIFF in very young animals even in 7–14 days. PAGET (*Lect. on Surg. Path.*) found in two cases the first traces of returning sensibility in about 15 days. After division of the facial nerve (in resection of the jaw) paralysis of the muscles of the face usually diminishes only after 2–3 months.

The conduction of nerves in a double sense has been experimentally demonstrated by the union of the hypoglossal nerve with the lingual (BIDDER, 1842; PHILIPPEAUX and VULPIAN, 1863; ROSENTHAL, 1864).

NÉLATON (1863) and LAUGIER (1864) have in man recommended suture of nerves for the quicker appearance of function; it has been followed by this result only in sensory nerves. According to LAUGIER, by the suture motion has become possible in two days (?). According to A. WAGNER, SCHUH, NUSSBAUM, and SZYMANOWSKI (*Prag. Vjschr.*, 1865, IV., p. 52) conduction in sensory nerves is only partly destroyed after neurectomy, or is interrupted for only a few days. Conduction in sensory nerves may occur indirectly, without union of the ends of the divided nerve. This conduction through anastomotic nerve-branches can, according to SZYMANOWSKI, be shown : a. by anatomical preparation; b. by sense of pain, which is felt by cutting, sometimes after division of the central end through the peripheric; c. by the fact, that only rarely is sensibility immediately and wholly destroyed by neurectomy of the nerves of the face. Etc. Physiologists have made similar observations with regard to the splanchnic nerve.

ARLOING and TRIPIER (*Arch. de physiol.*, 1869, p. 33) have made probable the presence of collateral anastomoses of the ends of the cutaneous nerves in certain mixed nerves of the arm. This would explain in nerve-section a vicarious conduction of sensitive impressions (in place of the so-called recurrent sensibility, assumed by many).

After that PFLÜGER had shown, that the epithelia of the salivary glands of the mouth, of the pancreas, liver, are terminal organs of nerve-fibres, this holds good also for all true secretory glands. Very probably all true epithelia, at least in their young state, are connected with nerve-fibres. (The sudden turning gray of hair as a result of emotion.) (*Arch. f. d. ges. Phys.*, 1869, 2. et 3. H., p. 190.)

REGENERATION OF GANGLIA.

That of the substance of the brain and spinal cord has not yet been certainly shown. Regeneration may, without further evidence, be concluded from the often observed restoration of function.

According to VALENTINE and WALTER (*De regener. gangl.*, Bonn, 1853), a regeneration of ganglion-cells occurs in animals after extirpation of ganglia. SCHRADER and SCHIFF did not find this confirmed. ARNEMANN, BROWN-SÉQUARD and H. MÜLLER observed in animals a regeneration of the lower portion of the spinal cord. SCHIFF observed the same after division of different parts of the spinal cord and brain. MASIUS and v. LAIR (*Med. Ctrlbl.*, 1869, No. 39) observed in frogs an anatomical and functional restoration of the spinal cord (pieces from 1 to 2 mm. long were resected). It required about six months, and occurred in a manner similar to that after division of nerve-fibres. VOIT (*Münchn. acad. Ber.*, 1868) observed in doves a new-formation of brain-substance with restoration of its activity.

H. DEMME (*Militär.-chir.-Studien*, 1861, I., p. 55) regards as probable a kind of immediate union in the central organs of the nervous system in incised and punctured wounds. In injuries of nerves connected with loss of substance, there is a filling up by means of interstitial cicatricial tissue. Once D. observed a regeneration of true nerve-substance in the central organs : it arises by free formation of primitive tubes within the connective-tissue intermediate substance.

B. HYPERTROPHY OF NERVES

occurs sometimes in hypertrophy of the organs concerned (as well of the extremities, as of the heart), but (except in the uterus, where it is physiological) never appears to affect the primitive fibres of the nerves, but only their connective tissue. However, a true hypertrophy of nerves probably occurs in the retina : it consists in thickening of the primitive tubes or in fibres formerly without medulla becoming medullary.

C. NERVOUS TUMOR, TRUE NEUROMA,

consists of vascular connective tissue in for the most part preponderating quantity, and of nerve-fibres ; the latter are rarely parallel, for the most part branched and closely interwoven, broad or small, mostly medullated, rarely without medulla ; usually without connection with the fibres of the affected nerve.

Many neuromata contain almost only gray, non-medullated nerve-fibres recognizable with difficulty in their bed of connective tissue : neuroma AMYELINICUM in opposition to n. MYELINICUM.

VIRCHOW distinguishes the pure neuromata, in which the nervous elements preponderate, the teleangiectatic neuromata, and, according to the kind of interstitial tissue, the fibrous, glious, and mucous neuromata.

The so-called neur. cirsoidenm s. plexiforme is characterized by the fact, that the nerve-fibres and bundles form, to the naked eye, irregular coils. It occurs most often in the temporal and cervical regions ; it is for the most part or always congenital. Consult VERNEUIL, *Bull. de la soc. anat.* de Paris, 1857, p. 25.—BILLROTH, *Arch. f. klin. Chir.*, IV., p. 547 ; XI., p. 232.—BRUNS, *Virch. Arch.*, L., p. 80.

According to FÖRSTER (*Würzb. med. Ztschr.*, II., p. 103) the nerve-fibres of neuroma proceed from spindle-shaped cells, which arise in the connective tissue, elongate, fuse one with another by their points and gradually receive contents similar to the medulla of nerves. HELLER (*Virch. Arch.*, 1868, XLIV., p. 338).—GENERSICH, *Ib.*, LI., p. 15.

Neuroma occurs in the course of one or more peripheral, for the most part spinal, rarely cerebral and sympathetic nerves, in varying number, and usually as small, rounded, smooth, sharply defined, usually partly solid tumors. It is also found at the cut end of nerves in amputation-stumps.

Neuromata are sometimes congenital, sometimes of traumatic origin. For the majority no CAUSE of origin is known.

The GROWTH of neuromata is for the most part slow, and they rarely reach large dimensions. The limiting tissues become affected only through

pressure, not by metamorphosis into neuromal tissue. They rarely retro-grade, metastases are not observed.

Nerve-fibres have sometimes been found in pseudo-membranes of the pleura. In tumors proper no new-formation of them seems to occur.

In cystoids of the ovaries, testicles, in tumors of the sacrum, medullary substance of nerves has a few times been found, especially gray substance, without connection with normal nerve-fibres.

Observations of GRAY, VERNEUIL, and VIRCHOW.

In the wall of the cranial cavity there sometimes occur tumors of vary-ing size, for the most part simple, consisting of brain-substance, which tumors probably are congenital.

Heterotopia of gray substance within medullary substance has been described by MESCHEDE (*Virch. Arch.*, XXXVII., p. 567) and VIRCHOW (*Ib.*, XXXVIII., p. 136). MESCHEDE (*Ztschr. f. Psych.*, XXI., p. 481) found in an idiot and epileptic per-son 19 years old a new-formation of gray brain-substance, not only in the surface of the ventricles, but also in the layers of white brain-substance bordering on the cor-*tex. Cases of heterotopia of gray substance in the medullary body of the hemi-spheres of the cerebellum : see MESCHEDE, *Virch. Arch.*, LVI., p. 82. Hyperplasia of gray substance of the brain, in the medullary body of the vermis cerebelli : see MESCHEDE, *Ib.*, p. 97.

TUBERCULA DOLOROSA are a for the most part subcutaneous movable tumors, the skin over them not at all or but little prominent, which of themselves or by pressure give rise to very severe pains. They are only in part neuromata, more often fibro-mata, etc.

X. HETEROPLASIÆ OR HETEROLOGOUS NEW-FORMATIONS OF CONNECTIVE TISSUE, AND ANALOGOUS TISSUES.

The new-formations considered hitherto are the so-called homœoplasiæ or HOMOLOGOUS NEW-FORMATIONS, *i.e.*, they all follow, in some or almost all the modes of their occurrence, physiological types ; so that they are either entirely the same (regenerations, many hypertrophies), or their similarity easily suggests itself (many hypertrophies, tumors).

The HETEROPLASIÆ hereafter to be considered, or HETEROLOGOUS NEW-FORMATIONS DEPART FROM THEIR PHYSIOLOGICAL TYPES IN SO MANY WAYS, that a separate consideration of them is necessary or advisable. But gradual transitions are in part also found in them, partly to the new-forma-tions already given, especially the tumorous, to many hypertrophies and to chronic inflammations, partly to the new-formations of cytogenic tissue to be considered hereafter.

The new-formations belonging here proceed always from connective tissue and from analogous tissues, especially endothelium, never from epithelium.

1. SARCOMA.

(Fibro-cellular tumor. Tumeur fibroplastique. Fibro-nucleated tumor.)

ABERNETHY, *Surgical Obs. ; Classification of Tumors*, Lond. 1804.--J. MÜLLER, *Ueb. d. fein. Bau*, etc., *der krkh. Geschw.*, 1838, p. 7, 21, etc.—LEBERT, *Phys. path.*, 1845, II., p. 120 ; *Abhandl.*, 1848.—VIRCHOW, *Arch.*, 1847, I., p. 195 et 470 ; *Die krkh. Geschw.*, II., p. 170.—REINHARDT, *Path.-anat. Unters.*, 1852, p. 122.— PAGET, *Lect. on Surg. Path.*, 1853, II., p. 151, 155, 212.—BILLROTH, *Virch. Arch.*, 1856, IX., p. 172 ; XVIII., p. 82.—VOLKMANN, *Virch. Arch.*, 1857, XII., p. 27.— RINDFLEISCH, *Lehrb. d. path. Gewebel.*, 1866, p. 119 ; 1873, p. 103.—NEUMANN, *Arch. d. Heilk.*, 1871, XXII., p. 66 ; 1872, XIII., p. 305.

(Consult besides the text-books of surgery and the literature of tumors generally.) In that which follows I have adopted especially VIRCHOW's description of sarcoma.

Sarcoma is a tumorous new-formation which belongs to the group of CONNECTIVE-SUBSTANCE TUMORS (fibroma, myxoma, osteoma, glioma, etc.), as these are always vascular, but is distinguished from sharply defined species of this group by the PREPONDERATING DEVELOPMENT OF THE CELLULAR ELEMENTS AS WELL IN SIZE AS IN NUMBER. Consequently, sarcoma is: or, and by far the most frequently, a SARCOMA FIBROSUM, fibrosarcoma, fibrous sarcoma; or, a SARC. MUCOSUM s. gelatinosum, myxosarcoma, mucous sarcoma; or, a S. GLIOSUM, glio-sarcoma; or, a S. CARTILAGINOSUM, chondro-sarcoma, cartilaginous sarcoma; or, a s. OSTEOIDES, osteo-sarcoma, osteoid sarcoma.

It is not allowable to wholly abandon sarcoma as a special tumor and to regard each of the other species as a sarcomatous variety (as fibroma sarcomatosum, myxoma sarc., etc.); for many sarcomata pass directly from the stage of granulation into their higher forms of development, without having to exist as true connective tissue, mucous tissue, etc.; and a sarcoma, which is perhaps developed from a fibroma, myxoma, etc., later by infection generates daughter-tumors, which are not at first fibromata, myxomata, etc., but immediately become sarcomata. Nevertheless the observer is not infrequently in doubt whether he should call a tumor a fibrous sarcoma or a fibroma, etc. Still more difficult is it to draw the boundary line between many small and round cell sarcomata, on the one hand, and many lymphomata, non-epithelial medullar tumors, etc., on the other. (See Cancer.)

The CELLS of sarcoma, its most important element, are very different in form, size, etc., but show in general either further development, or only hypertrophic states of the cells of the forms of connective-tissue substance. In many sarcomata they are small. They are, however, for the most part distinguished by their considerable SIZE, still more by the size of their nucleus and nucleolus. With respect to FORM the cells are round, spindle-shaped, or stellate. The spindle-shaped cells appear in many cases wholly like the endothelial cells of serous membranes, vessels, etc., as well as connective-tissue corpuscles; nuclear, very delicate, transparent, thin, not granular, easily folded plates, which are sometimes invisible, and inseparably connected. In many sarcomata cells occur to a great extent, which consist half of protoplasm, half of fibrillar connective-tissue substance, and the firm masses represent the matrix of every connective tissue forming itself anew: fibroplastic corpuscles or fibro-blasts (see p. 373). The fibro-blasts are at first round, and gradually become spindle-shaped. The formed elements are elongated, and consist of a medium-sized, broad, for the most part flattened cell-body which is formed of granular protoplasm and provided with a vesicular nucleus and nucleolus, and has two bipolar processes, the substance of which shows a more or less advanced metamorphosis of the protoplasm into bundles of fibrillæ. According to the form of the cells are distinguished the STELLATE or RETIFORM CELL, and the ROUND CELL SARCOMA; according to their SIZE, the LARGE and the SMALL CELL SARCOMA. Often only one of these forms occurs in the same sarcoma, but often one sarcoma contains them all, sometimes in different sections, sometimes close by side' of one another. Sarcoma cells are mostly uncolored, rarely in different degrees pigmented: MELANO-SARCOMA, PIGMENT-SARCOMA.

The STELLATE or RETICULAR CELL SARCOMA is distinguished by the strong development and the number of the stellate cells, but often shows transitions to other sarcomata. It occurs especially as melano-, myxo- and glio-sarcoma.

The SPINDLE or FIBRE CELL SARCOMA (FIBROPLASTIC TUMOR, plasmoma), the MOST FREQUENT form of sarcoma, consists of spindle-shaped cells,

which show a comparatively thick body with large, oval or round, for the most part single, more rarely multiple nucleus and two, sometimes very long processes. Sometimes the processes are numerous, often branched. The free nuclei occurring in many of these sarcomata have for the most part become free only through destruction of cells : so-called FIBRO-NUCLEATED SARCOMA. The spindle-shaped cells are usually more or less parallel ; they are separated by intercellular substance or are in almost immediate contact. Sometimes the spindle-shaped cells are concentrically arranged, or like the layers of an onion, around a clear, soft or calcified central point. Out of the cells are often formed larger trabeculæ, lamellæ or bundles : LAMELLAR or FASCICULAR sarcoma. These sometimes form a radiate structure. More often many central points exist, an interweaving, a trabecular arrangement : TRABECULAR SARCOMA. Section shows then longitudinal, transverse and oblique section of the trabeculæ, which in microscopical pictures may lead to their confusion with carcinoma. In many sarcomata the spindle-shaped cells have a similarity to young transversely striated, as well as with smooth muscular fibres, so that, especially with scanty or wholly absent intercellular substance, they may be confused with myomata. Most spindle-cell sarcomata belong to fibro-sarcomata.

The ROUND CELL SARCOMA is found most frequently as glio- and myxo-sarcoma (many forms of the former are almost like neuroglia—many of the latter are very similar to bone-marrow : myxo-sarcoma medullosum s. myelodes), less often as fibro-sarcoma, etc. In glio-sarcoma the for the most part small elements often lie in connected rows, so that its appearance is characterized .by a radiating striation : RADIATE SARCOMA. The cells are usually so frail, that only the so-called free, mostly pale, cell-like nuclei with large nucleoli appear ; in fatty metamorphosis, as well as in pigmentation, the cell-contour for the most part appears very distinct. The cells sometimes have two and more nuclei. Their contents are finely granular. Their form is spherical or irregularly rounded or oval ; their size exceeds for the most part that of mucous corpuscles. The cells are always, if also with scanty and sometimes very soft basis substance, separated from one another. Transitions to medullary cancer arise in the latter case, or through the presence of vessels, especially if these have stronger connective-tissue sheaths, or through the remains of the earlier tissue.

MONRO's milt-like tumor belongs in part to the round-cell sarcomata ; also BILLROTH's sarcoma with granulation-like structure : the small, round cell with large nuclei lie in an amorphous intermediate substance—especially in the periosteum and cerebral meninges ;—LANGENBECK's scrofulous sarcoma ;—RINDFLEISCH's lymph-gland-like sarcoma : the cells lie in the spaces of a delicate net-work, analogous to that of the lymph-glands, follicles, etc.—especially in the subcutaneous and intermuscular tissues.

The SMALL CELL SARCOMA has the greatest similarity with glioma, lymphoma and certain forms of granulations, regarded pathologically ; with the granular layers of the brain and retina, sometimes also with the medullary masses of the lymph-glands and young bone-marrow, regarded physiologically. The cells are round or spindle-shaped. Between them there is a scanty homogeneous substance. These sarcomata belong essentially to glio- and myxo-sarcoma, and occur in the sheaths of vessels and nerves, in the skin, etc.

The LARGE CELL SARCOMATA are for the most part fibro- and melano-sarcomata. The spindle-cells become very large ; between them is a scanty, homogeneous, or fibrous substance.

The GIANT-CELL SARCOMATA (myelo-plastic tumors), most frequently the myeloid sarcomata, contain large cells with a varying number (20, 30 to 100) of, for the most part quite large, but somewhat pale, nuclei inclosing one or many nucleoli, which latter lie in a finely granular, sometimes yellowish, often very dense and less transparent substance. Therewith are often found transitions to common cells with single nucleus.

The PIGMENT SARCOMA contains within its cells scanty or abundant, very small or larger, light brownish or blackish molecules. It proceeds more often from the choroid and skin. Eventually secondary sarcomata are likewise often pigmented, rarely without pigment.

On a melanoma of the cornea, consult LANGHANS, *Virch. Arch.*, LI., p. 117.

The INTERCELLULAR SUBSTANCE of sarcomata is rarely pure connective tissue, but for the most part contains a tolerably large quantity of albuminous, caseinous, or mucinous elements. It is besides homogeneous, or granular, or fibrillar. The basis substance is FIBRILLAR most often in fibro-sarcoma. The fibrillæ are usually denser, stiffer and more stretched than in common loose connective tissue. The basis substance is granular most often in the glio-sarcomata, also in many small cell myxo-sarcomata. HOMOGENEOUS intercellular substance is sometimes hyaline, gelatinous, as in many myxo-sarcomata especially of bone-marrow, but where it for the most part is traversed by fibres; sometimes the basis substance is very dense, like hyaline cartilage, as in many fibro-sarcomata, especially of the brain; sometimes later it thus becomes dense and then leads to calcification and ossification, as in many osteo-sarcomata. Not infrequently all three kinds of basis substance occur beside one another.

The relation between the basis substance and the cells of sarcoma is usually such, that the latter are arranged parallel with the former, and are firmly imbedded in it. But not infrequently the connection between the for the most part small round cells and the basis substance is so loose, that in common or rather in pencilled sections there appears a fine net-work, which resembles that of cytogenic tissue : so-called GRANULATION-LIKE or LYMPHOID or LYMPHADENOID SARCOMA. Or the cells (pale or pigmented) of sarcoma reach in the subcutaneous connective tissue, muscles, bones, eyes, etc., a greater development, become more like epithelium and distend the basis substance into distinct spaces or alveoli : so-called ALVEO-LAR SARCOMA, SARCOMA CARCINOMATODES. If the tumors are pigmented, like pigmented round cells, single or accumulated, but not with an alveolar arrangement, will often be found in the stroma.

Consult concerning the latter, BILLROTH, *Arch. f. klin. Chir.*, 1869, XI., 1. H., p. 244. RINDFLEISCH, *Lehrb.*, 1871, p. 112. NEUMANN calls only those sarcomata alveolar, the cells of which, deposited in the meshes of the alveolar stroma, are characterized by the tendency of their protoplasm to metamorphosis in intercellular substance like connective-substance cells. (See Cancer.)

VESSELS are an integral constituent of all sarcomata. They show sometimes no departure from their usual structure, sometimes their wall is wholly, or with exception of the most internal layer metamorphosed into sarcomatous tissue. The vessels are sometimes present in usual number; sometimes they so far preponderate in number and width, that whole portions assume a peculiar appearance : SARCOMA TELEANGIECTODES. This is very prone to internal and external hæmorrhages : SARC. HÆMORRHAGICUM. This may again become the starting-point for pigment formation, which must be distinguished from autochthonous pigment : proper melanotic, and

hæmorrhagic colored sarcomata. Many sarcomata show still a peculiar parenchymatous coloring, which belongs to certain tissue-elements, just as the color of muscles belongs to primitive muscular bundles.

Sarcomata occur most frequently in and under the skin : common large sarcomata ; so-called flesh-warts, *verrucæ corneæ s. molles ;* many pigment spots, congenital, so-called *nævus pigmentatus, spilus,* as myrmecine ; melano-sarcomata. Also between the muscles and on fasciæ (of the abdomen, back, and extremities), in the mediastinum and in the orbits ; on the periosteum, on the gums (so-called epulis), and in the interior of bones, especially of the ends of long tubular bones and of the lower jaw ; in the female mammæ, in the testicles ; the adventitia of vessels, in the sheaths of nerves. Rarely they are found in internal organs, especially the brain (common sarcomata and many so-called tubercles of the brain), spinal cord and its membranes, especially on the dura mater, in the lungs, liver, kidneys, pancreas, uterus, etc. In the lungs, liver, heart, mucous and serous membranes sarcomata occur for the most part only SECONDARILY, in lymph-glands primarily and with comparative rarity secondarily.

The ORIGIN of sarcoma takes place most often from common connective tissue, especially also from the adventitia of bloodvessels and the nerve-sheaths, or from an analogous tissue (mucous tissue, osseous tissue, etc.), for the most part in such a way, that at first by division, etc., of the cells there arises a kind of granulation tissue, usually with new-formation of blood-vessels, with or without new-formation of intermediate substance, or with partial destruction of the latter. Less often, in a similar manner, from parts or from the whole mass of a tumor of another kind of connective tissue, cartilage, etc.), there arises a sarcoma (transformation or degeneration).

LÜCKE, LAMBL, CORNIL-RANVIER, but especially ROBIN (*Journ. de l'anat. et de la phys.*, 1869, VI., p. 239), GOLGI (see Psammoma) and NEUMANN (*Arch. d. Heilk.*, 1872, XIII., p. 305) have shown, that many so-called spindle-cells of sarcomata appear, on closer examination, etc., similar to the endothelium of serous membranes, vessels, etc. Since also fixed connective-tissue corpuscles are, by RANVIER and BOLL, considered as endothelial cells, the connective-tissue character of sarcoma is corroborated by these more recent investigations, if perhaps an endothelial new-formation, an ENDOTHELIOMA (GOLGI) be left out of consideration. (Consult also MICHEL, *Arch. d. Heilk.*, 1873, XIV., p. 39.)

The INFLUENCE OF THE LOCALITY on sarcomata is clearly evident : osteoid sarcomata often appear on the surface of bones ; softer, medullary forms richer in cells, in the medullary cavity ; pigmented sarcomata often in the skin and choroid ; glio-sarcoma in nerve-centres ; firmer, especially fasciculated sarcomata with large spindle-cells, in fibrous membranes, especially fasciæ, in the sclerotic and dura-mater ; soft, gelatinous or pulpous sarcomata with very delicate intercellular substance preponderate in the glands. Secondary and primary sarcomata have in general the same character.

Sarcomata are MOSTLY SINGLE, tumorous, and very rarely multiple from the beginning. They are sometimes sharply circumscribed, rarely encapsuled, sometimes diffuse. Sometimes in the vicinity of the single tumorous sarcoma new nodules appear, which are connected with the old tumor, so that they then have the appearance of being lobes of the former. On the skin, on mucous and serous membranes sarcoma is sometimes polypoid in shape : polypous sarcoma.

The greater number of sarcomata are tumor-like. DIFFUSE SARCOMA, which has

the form of an infiltration or hypertrophy, occurs especially in the muscles, in the female breast, and in the testicles. The new-formation takes place in the interstitial connective tissue, while the muscular fibres, gland-cells, etc., for the most part undergo atrophy. Under certain conditions pre-existing cavities and canals dilate into cyst-like forms (so-called CYSTO-SARCOMA), especially in the mammæ.

Sarcomata are of very varying size; they are largest in the mediastina and in the extremities. They are rounded or irregular, spherical or flattened, on the surface uniform or lobed. Nothing general can be stated with respect to their consistence and the character of their cut surface.

With respect to consistence, sarcomata are HARD or SOFT: to the former belong in general steatoma or lardaceous tumor of the earlier writers, most cases of fibro-, chondro-, and osteo-sarcoma; to the latter the until now so-called fleshy tumors and their derivatives, medullary tumors, most cases of myxo-, glio-, and melano-sarcoma. Their consistence depends chiefly upon the character and abundance of the intercellular substance. Every variety of sarcoma may in parts, some may even throughout become so rich in cells and thereby so soft, that the special type of the mother-tissue is wholly lost: SARCOMA MEDULLARE (fibro-sarc. med., myxo-sarc. med., etc.), or, since the medullary depends upon the abundance of cells: sarc. multi-cellulare.

The further GENERAL PROPERTIES of sarcomata show great differences, especially with respect to the character of the sarcoma itself and the kind of organ affected.

Sarcomata are for the most part painless.

Their INFLUENCE ON THE ORGAN affected, and on the WHOLE ORGANISM depends chiefly upon their seat (brain, spinal cord, mediastinum, etc.), as well as upon their size, more rarely upon their metamorphoses.

All sarcomata which are very rich in cells, especially in small cells, are in high degree suspicious, and herein are the small cell glio- and myxo-sarcomata hardly inferior to the medullary cancer. Opposed to these are the fibro-sarcomata with colossal spindle-cells, and even the soft sarcomata with multi-nuclear giant-cells. Further, malignity depends upon the organ affected: sarcomata of the testicle tend much more to metastasis than those of the ovary; the spindle-cell sarcomata of the brain are almost without exception solitary, those of the bones more often multiple; sarcomata of fasciæ afford a more favorable prognosis than those of mucous membranes. An especially great extent is reached by the for the most part very cellular sarcomata of the mediastinum, orbits, the deep-lying cervical sarcomata, many retro-peritoneal sarcomata, many lying deep in the extremities, especially in the thigh, many diffuse sarcomata of the uterus. The pigmented medullary sarcomata of the interior of the eye are by their progress to the neighboring structures, especially the cerebral pia mater, and by their metastases, especially dangerous.

The GROWTH of sarcoma is sometimes from beginning to end slow, sometimes at first rapid, later slow, sometimes rapid to the end.

Growth takes place sometimes in only one direction, sometimes in all directions along the tissues from which the sarcoma took its rise: e.g., along the periosteum, or mucous membrane in the nasal cavities and in all cavities connected therewith. Growth takes place with especial preference along the small bloodvessels. Many sarcomata are for a long time sequestrated by more resistant surrounding structures: thus those of the articular extremities in the articular cartilage, others by fibrous membranes (periosteum, fasciæ, sclerotic), by the walls of large vessels. After overcoming these obstacles, growth then usually becomes rapid. Sarcomata either remain always circumscribed, or become in parts or throughout diffuse, i.e., pass to all parts and tissues of the vicinity.

I saw a man, 30 years old, affected by an ACUTE SARCOMA of the peritoneum with simultaneous peritonitis run its course in hardly six weeks—analogous to the cases of acute miliary tuberculosis and acute carcinosis.

Complete cure sometimes follows EXTIRPATION, at other times there is RECURRENCE months or years thereafter, in the cicatrix, more rarely in the proper lymph-glands (hence the name: recurring fibroid). After operation of the latter, cure sometimes results, sometimes one or many return, in some cases as many as twenty. Even now perfect cure is still possible. But, more frequently, the recurring tumors are always richer in cells and diffuse, and sarcoma appears in the vicinity of the mother-nodules, or the proper lymph-glands (which, however, not infrequently remain perfectly free), or in internal organs, most often in the lungs, also in the liver and kidneys (thus especially in sarcomata of bones).

The RETROGRADE METAMORPHOSES of sarcoma, which occur comparatively often and are for the most part intense, are: inflammation, sometimes with consecutive ulceration or ichorization; laceration of vessels; simple atrophy and thereby formation of yellow foci-like tubercle; fatty metamorphosis sometimes with consecutive softening (and in consequence of it partial resorption, or ulceration, or cyst-formation), sometimes with subsequent cheesy transformation or tuberculization; calcification.

The CAUSES of sarcoma remain almost always unknown. Predisposed thereto are riper age, as well as parts, which had been once or oftener exposed to injuries or other irritations.

On the possible relations of sarcoma with constitutional syphilis, see ESMARCH (v. WASMER, *Beitr. z. Aetiol. u. Ther. d. Sarcoms.* Kiel. Diss., 1872).

APPENDIX.

PSAMMOMA. SAND-TUMOR.

VIRCHOW, *Die krankh. Geschw.*, II., p. 107.—CORNIL et RANVIER, *Man. d'hist. path.*, 1869, p. 133.—GOLGI, *Sulla strutt. e sulla sviluppo degli Psammomi.* Pavia, 1869.—SCHÜPPEL, *Arch. d. Heilk.*, X., p. 410.—STEUDENER, *Virch. Arch.*, L., p. 222.—ARNOLD, *Ib.*, 1871, LII., p. 449.—NEUMANN, *Arch. d. Heilk.*, XIII., p. 305.

Psammoma is a for the most part very vascular tumor of fibromatous, myxomatous, or most often of cellulo-sarcomatous nature, which is distinguished by the constant occurrence of variously abundant, round or rounded, concentrically laminated chalky masses. The latter resembles the cerebral sand occurring constantly in the pineal gland, often in the choroid plexus, etc. The tumor occurs not infrequently, single or multiple, on the dura mater cerebri and in the choroid plexus, less often in the brain and other parts of the body (lymph-glands, spleen, peritoneum, orbits, etc.). Their CONSEQUENCES depend especially upon their seat.

VIRCHOW first described psammoma. In SCHÜPPEL's case there was at the same time a colossal thickening of the pericranium. According to S. the bloodvessels, present in great abundance, determine the starting-point of the tumor's development, and also from them proceed the sand-bodies; their organic base is the obsolete vascular processes. Also, according to CORNIL and RANVIER, the sand-bodies of the choroid plexus arise within the vascular buds or ampulla-form dilatations of the vessels of the plexus as true phleboliths. They likewise appear in like tumors of the dura mater (so-called *sarcômes angiolithiques*). STEUDENER, on the other hand, regards those tumors only as psammoma, whose tissue by its slow growth and

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almost want of tendency to multiplicity stands midway between fibroma proper and solid spindle-cell sarcoma. Into this tissue numerous chalky bodies of the appearance and properties of cerebral sand are deposited. According to ARNOLD, chalky globules and rods are formed by petrifaction of the contents of the vessels, by local petrifaction of the vessel itself, by local increase and petrifaction of the adventitia; also by calcification of connective-tissue bundles, by that of cell-groups; a part finally are true concretions of non-organic origin.

2. SYPHILOMA.

(Tuberculum s. gumma syphiliticum. Tumor gummosus, gummy tumor.)

RICORD, *Traité prat. des mal. vénér.*, 1838.—DITTRICH, *Prag. VVjschr.*, 1849, I., II.—BÄRENSPRUNG, *Deutsche Klin.*, 1858, No. 17; *Ann. d. Char.*, IX., p. 110.—VIRCHOW, *Arch.*, 1858, XV., p. 217; *Die krkh. Geschw.*, II., p. 393.—WILKS, *Transact. of Path. Soc., Lond.*, 1858, et seq.—LEBERT, *Hlb. d. pract. Med.*, 1859, I., p. 370.—CHASSAIGNAC, *Allg. Wien. med. Ztg.* 1859, No. 50.—ROBIN, In VAN ORDT, *Des tumeurs gommeuses*, 1859, No. 44.—STEENBERG, *D. syphil. Hjernelidelse*, 1860.—BUHL (-LINDWURM), *Würzb. med. Ztschr.*, 1863, III., p. 154.—E. WAGNER, *Arch. d. Heilk.*, 1863, IV., p. 1, 161, 221, 356; V., p. 121; *Univ.-Programm.*, 1863; *De syphilomate ventriculi.*—WEGNER, *Virch. Arch.*, L., p. 395. — OEDMANNSON, *Nord. Medic. Ark.*, 1871, I., No. 18.
Consult besides, the literature of Syphilis in general; the text-books of pathological anatomy of ROKITANSKY, RINDFLEISCH, KLEBS, GREEN.

SYPHILOMA is a new-formation of varying extent, dependent upon constitutional syphilis, apparently circumscribed or diffuse, and occurring in almost all tissues and organs. Its essential elements are similar to the colorless blood-corpuscles, for the most part cells with a single and large nucleus and free nuclei, which, single or few in number, are imbedded in a connective tissue poor in vessels.

Syphiloma shows manifold TRANSITIONS, for the most part recognizable in the fresh state, to many forms of granulation tissue and to many sarcomata.

Syphiloma occurs in all vascular tissues and organs: most frequently in the skin, especially of the genitals and anus (indurated chancre, broad condylomata, larger so-called gummata), in the subjacent parts, especially the subcutaneous connective tissue, in the muscles, periosteum and osseous tissue, liver; more rarely in the testicles, epididymis and its membranes; in the dura mater and pia mater; in the mucous membrane and other membranes of the mouth, tongue, throat, stomach, large and small intestines, in those of the larynx, trachea and bronchi; in the spleen, pancreas, lungs, brain, heart and great vessels, thyroid gland, kidneys.

Syphiloma, IN THE FRESH STATE, is represented by a grayish red, soft, homogeneous mass, sometimes presenting scattered blood-points, and without fluid, or affording a scanty mucous, clear or clouded liquor. It either forms, in membranes as well as in parenchymata, nodular masses of the most varying size, from that of a millet-seed to that of the fist, of a round, rounded, or irregular form, sometimes with an apparently sharply defined boundary; or it assumes, especially in membranes, more rarely in parenchymata (lungs, liver, spleen), the form of DIFFUSE INFILTRATIONS of the most varying extent; or finally, nodular masses occur in a diffuse infiltration (lungs, liver).

After a varying existence, syphiloma passes either into SIMPLE ATROPHY with scanty fatty metamorphosis, or into ULCERATION or formation of cavities; or both occur simultaneously. In the former case the new-formation gradually becomes gray or yellowish-gray, firmer, drier, juiceless;

at first for the most part only in the centre, more rarely also in the periphery. The limit between the reddish gray and yellow parts is usually distinct. In the other case irregularly depressed ulcers of varying size occur on the surface of the skin or mucous membrane; in parenchymatous organs, as well as in nodular infiltration of superficial tissues cavities are formed, which contain in a serous or mucous liquid the remains of the firmer or cheesy mass.

MICROSCOPICALLY, syphiloma consists of cells or nuclei, or of both at the same time, so that sometimes the former, sometimes the latter exceed in number. Young syphilomata, as well as the peripheral parts of older ones, contain for the most part only nuclei, or nuclei and isolated cells; the older syphilomata, not yet very atrophic, consist for the most part only of cells or of cells with few nuclei. The NUCLEI offer nothing characteristic. They are from 0.01 to 0.02 mm. large, round or rounded, or somewhat angular, rather rarely show processes of division, and contain for the most part a distinct nucleolus. The CELLS resemble most uni-nucleate colorless blood-corpuscles. Their size varies, however, sometimes between 0.01 and 0.03 mm.; some are even still larger. Their form is for the most part round, sometimes oval, or angular with flattened sides when they press against one another. The cell-membrane is almost always distinct, its contents moderately granular; the nucleus, centrally or eccentrically located, is for the most part single, rarely double, and for the most part comparatively large.

The relation of the cells and nuclei to the surrounding substance is characteristic. The former lie oftenest isolated in very small hollow spaces surrounded by connective tissue. The latter is for the most part so scanty, that between the single cells only fine connective-tissue fibrillæ are visible. Besides the forms named, there is not infrequently found also those, where more than one cell, ten and even more cells are within one alveolus. If very fine sections be brushed, there will appear after removal of the cells either true alveoli, *i.e.*, sharply defined, empty, round or oval spaces; or in the previously apparently simple alveolus are seen the finest fibrillæ, which sometimes again form very small and distinct alveoli within the large alveoli.

The connective tissue in which cells and nuclei are imbedded is sometimes present in large quantity, as often in the corium of the skin and mucous membranes, in the connecting cellular matter of organs or parts of organs; sometimes it is scanty, as in membranes of organic muscular fibres, in elastic membranes, in parenchymata poor in connective tissue (liver, lungs, brain, etc.). That connective tissue occurs sometimes very abundantly in older syphilomata, so that apparently only callous masses are present, is the consequence of simple and fatty atrophy and subsequent resorption of the cellular elements. The capillaries and larger vessels of the cellular infiltrated tissue appear to suffer only slight changes.

BIESIADECKI (*Unters.*, 1872, p. 5) found the lymphatics in an indurated chancre dilated and filled with fluid and cells.

The most frequent METAMORPHOSIS of syphiloma is SIMPLE ATROPHY of the cells and nuclei, for the most part simultaneously with slight, rarely with high degrees of FATTY METAMORPHOSIS. Both metamorphoses affect, for the most part at first, the central and oldest portion of the new-formation, whence they always extend outward toward the periphery, so that the latter sometimes only microscopically shows elements still unchanged.

Through these metamorphoses ulcers arise, in diffuse superficial extension on the skin and mucous membranes, cavern-like cavities in moderate nodular infiltration in membranes and parenchymata. If this atrophy happen remote from the surface of the skin or mucous membrane, and the highest layers of these be only little or not at all infiltrated, there will appear on their surface POINTS RESEMBLING CICATRICES, OR WHICH ARE TRULY CICATRICIAL. Hæmorrhages, and metamorphoses of the extravasation into pigment are only rarely found in syphiloma.

Connective tissue, especially the adventitia of vessels, forms the point of departure of syphiloma. In some organs, which are especially poor in connective tissue, the cells and nuclei of syphiloma arise by the growth of the nuclei of the capillaries, with subsequent fibrous metamorphosis of the capillary wall: thus in the brain, liver, etc.

In most cases the cells and nuclei are the only new-formation of syphiloma. But not infrequently a simultaneous new-formation of connective tissue undoubtedly takes place, especially in parenchymatous organs poor in connective tissue (brain, liver, spleen, etc.).

The hardness of indurated chancre depends not only on the dryness of the tissue and in the cellular infiltration, but also on a new-formation of connective-tissue fibres (BIESIADECKI, l. c., p. 7).

Most probably there also occurs a peculiar affection of the arteries in constitutional syphilis: this has been investigated especially with respect to the brain (PASSAVANT, HEUBNER, FLECHSIG).

The INFLUENCE of syphiloma on the ORGANISM depends upon the fact, that the affected portions of the membranes and parenchymata are more or less incapable of function: partly upon the deposit of cells and especially of nuclei; upon compression or secondary atrophy of the capillaries, gland-cells, nerve-fibres, ganglion-cells, etc. In canals (air-passages, etc.) there results, besides, a contraction of them, which exerts an influence varying with the locality, extent of the contraction, etc. (so-called syphilitic stenosis of the larynx, trachea, portal vein); in cavities containing air these become smaller even to a complete evacuation of the air (so-called syphilitic pneumonia). In consequence of cicatrization there result the so-called lobings of the liver, tongue, tonsils, etc.

If the membrane affected form at the same time a matrix for the parts supported by it, e.g., epithelium, the nutrition of this will suffer, especially if cellular infiltration affects chiefly the superficial layers. This is seen in the common portions of the skin, mucous membrane of the mouth and throat; also in the nails (syphilitic onychia).

In rare cases, after a long duration of common syphiloma, there occurs one of the very numerous miliary new-formations similar to general miliary tuberculosis and carcinosis, and spread over many organs. These new-formations at first show the structure of syphiloma, and furnish a form clinically similar to acute tuberculosis.

SYPHILOMA IN ITS RELATIONS TO OTHER NEW-FORMATIONS differs in most respects essentially from them all.

In the first place, syphiloma is essentially different ÆTIOLOGICALLY. The predisposition thereto is general, like pus-formation. Syphiloma occurs at every age; it is especially frequent in the fœtus, in each sex. (Concerning bone-syphilis occurring in the fœtus: so-called osteochondritis syphilitica at the points of transition of the diaphyses to epiphysal cartilages—consult WEGNER; WALDEYER and KÖBNER, *Virch. Arch.*, LV., p. 367.*)—The exciting causes of syphiloma are better known than those of other new-formations.

* Consult R. W. TAYLOR, *Syphilitic Lesions of the Osseous System in Infants and Young Children*. N. Y., 1875.—[ED.]

The SYMPTOMATOLOGY also of syphiloma is in many cases very distinct. In general the symptoms in so-called secondary syphilis are acute; the pathological disturbances are partly congestive hyperæmia, partly superficial, in part deeper inflammations with sometimes scanty, sometimes abundant exudation. On the other hand, in the so-called tertiary period the symptoms are on the average chronic: the new-formations, as well as the sometimes resulting gangrenous processes, appear slowly, last a longer time and retrograde slowly, for the most part with loss of substance.

The GROSS and MICROSCOPICAL TEXTURE of syphiloma are in most cases so characteristic, that confusion with other new-formations is impossible. Syphiloma furnishes most analogies in structure, as well as in the form of its occurrence, growth, origin, influence on the mother-tissue, on the surrounding tissues and the whole organism : in its diffuse form, with many diffuse or so-called infiltrated suppurations, with the granulation-tissue in so-called *tumor albus* of the joints, with granular and trachomatous affections of mucous membranes, with the diffuse new-formation of tubercle, lymphoma, cancer ; in its appearance as tumors with many abscesses, sarcomata, and cancers. A comparison with lupus and tubercle is inadmissible.

Whilst I refer to the literature of syphiloma of individual tissues and organs I give prominence only to many affections, which, partly on account of the simultaneous occurrence of other syphilitic affections, in part finally from the gross anatomical and especially histological character belong doubtless to syphiloma. They are : many cases of lupus, many cutaneous ulcers belonging to no known affection, many peculiar affections of the dura mater and pia mater, many tubercles of the meninges and brain, many laryngeal tumors, the so-called white hepatization of the lungs of the fœtus, some cases of peculiar pulmonary tubercules, many affections of the liver until now referred to inflammation with formation of cicatrix, many cases of so-called *glossitis dissecans*, many tubercles of the spleen, many cases of so-called hypertrophy of all the membranes of the stomach, many intestinal ulcers.

On SYPHILIS OF THE PLACENTA consult : VIRCHOW, *Arch.*, XXI., p. 118.—GUS-SEROW-KLEBS, *Ib.*, XXVII., p. 321.—R. MAIER, *Ib.*, XLV., p. 317.—SLAVIANSKY, *Prag. Vtljschr.*, 1871, CIX., p. 130.—KLEINWÄCHTER. *Ib.*, CXIV., p. 93.—OED-MANNSON, *Nord. med. Arch.*, I., 4. H., p. 73.—ERCOLANI, *Della malatie della placenta*, 1871.—HENNIG, *Stud. üb. d. Bau d. menschl. Plac.*, 1872.

According to FRÄNKEL (*Arch. f. Gynäk.*, 1873, V., p. 1) there are many forms of syphilis affecting the placenta. If the mother remains healthy and the syphilis is conveyed by the father directly to the ovum, the villi of the fœtal placenta will show deforming cellular granulation growth with obliteration of the vessels, more often also strong growth of the epithelium of the villi. If, on the other hand, the mother is syphilitic, there are three possibilities : *a.* the mother by the act of conception becomes syphilitic simultaneously with the fœtus: then for the most part there will arise in the placenta diffuse syphilis of the villi, sometimes also, endometritis placentaris ;—*b.* if already before conception or soon after, the mother becomes affected : the placenta will remain normal, or show *endometritis placentaris gummosa* or *decidualis ;—c.* if the mother becomes affected from the seventh to the tenth month : there will, for the most part, be a normal placenta and normal fœtus.

3. LUPUS.

BERGER, *Diss. de lupo.*, 1849.—MARTIN, *Illustr. med. Zeit.*, 1852, I.—POHL, *Virch. Arch.*, 1854, VI., p. 174.—MOHS, *De lupi forma et structura nonn:*, Lips., 1855.—AUSPITZ, *Oestr. med. Jahrb.*, 1864.—GEDDINGS, *Ber. d. k. Acad.*, 1868, LVII.—VIRCHOW, *Die krankh. Geschw.*, II., A., p. 482.—GÜTERBOCK, *Virch. Arch.*, 1871, LIII., p. 344.

LUPUS NEW-FORMATION consists of nuclei and cells, which form a diffuse or nodular infiltration of the corium of certain parts of the skin (especially of the face) and sometimes of the bordering mucous membranes. The new-formed nuclei have nothing characteristic; they are for the most part round, more rarely oval, small or of medium size. Cells are sometimes entirely wanting, or are present in slight quantity, or they form the chief element; they resemble sometimes uninuclear colorless blood-corpuscles, sometimes they are larger, rounded or irregular, sometimes they in part

resemble epithelium. All these elements lie for the most part in a scanty or somewhat abundant basis substance. Sometimes most of the above cells resemble common pus-cells. Sometimes spindle-shaped cells, similar to those of sarcoma, are more or less abundant. A new-formation of capillaries is still doubtful. The epithelium of the gland-ducts or glandular extremities and of the hair follicles, accumulates in large quantities, are concentrically laminated, and then are often macroscopically visible.

The elements of lupus show still further differences with respect to arrangement, extent, metamorphoses, etc. They most frequently form very small (to and above the size of a pea), rounded, reddish or brownish nodules, between which the skin or mucous membrane is not normal, but exhibits like changes in less degree. This uniform or nodular infiltration sometimes does not extend to the upper surface of the corium: the skin or mucous membrane above appears normal or shows a moderate scaling, until after a varying time the lupus elements are resorbed and there is left behind a smooth or radiating cicatrix. This is LUPUS NON EXEDENS; or if there occurs a more abundant exfoliation of the surface, LUPUS EXFOLIATIVUS. If the nodules or uniform infiltration are more marked, the new-formation is called LUPUS HYPERTROPHICUS. If the new-formed elements perish, after that they have reached the surface of the skin or mucous membrane, and ulcers result, which for the most are covered with crusts, their base consisting of lupus masses, then there arises LUPUS EXEDENS, vel EXULCERANS, vel RODENS, vel ESTHOMENOS.

From the above representation it follows, that not only the various kinds of lupus are founded only on the different modes of extension, various metamorphoses, etc., but the new-formation itself shows manifold analogies with many acute and chronic formations, with typhous and carcinomatous formations and especially with syphiloma. Of especially practical importance is the so-called SYPHILITIC LUPUS, which, if it occurs without other syphilitic affections, is only little or not at all characteristic, but yields to anti-syphilitic treatment.

RINDFLEISCH (*Lehrb.*, 1871, p. 290) regards lupus as a peculiar adenoma of the sebaceous and sweat glands: the body of the sebaceous gland becomes about five times larger, the root sheath of the hair presents here and there, in place of flat epidermal cells, large vesicular forms; the hair itself disappears, etc. The small cell infiltration is, according to R., secondary, according to others primary.

With AUSPITZ (l. c.), FRIEDLÄNDER (*Med. Ctrlbl.*, 1872, No. 43) also found that lupus stands histologically in a very near relation to scrofulo-tuberculous affections.

BUSCH (*Arch. f. klin. chir.*, 1872, XV., p. 48) describes an epithelioma-form of lupus. This agrees in structure most with the so-called yaws or framboesia, whilst also here at first there appear papulous and nodular, later soft, fungous, condylomatous excrescences. This form of lupus has its favorite seat in the extremities, especially their extensor side. Numerous processes and club-shaped projections, which have a blunt extremity or are branched dendritically, consisting wholly of epithelial cells, project from the surface into the common lupus tissue. The disease runs a very chronic course. It is followed, according to its extent, depth, etc., by necrosis of the bones, formation of strong, contracted cicatrices, etc., and almost always heals, and is therefore with respect to life, harmless.

4. LEPRA.

BOECK and DANIELLSEN, *Óm Spedalskhed*, 1847; *Traité de la spédalsked ou éléphantiasis des Grecs.* Paris, 1848.—FÖRSTER, *Path. Anat.*, 2. Aufl., I., p. 455.

LEPRA, ELEPHANTIASIS GRÆCORUM, LEPROSY, formerly spread over all Europe and also in Germany, is now found in Europe only in Iceland, Norway (SPEDALSKHED), the Baltic sea provinces of Russia, and in the countries bordering on the Caspian and Mediterranean seas; besides in Asia Minor, Arabia, Egypt, India, China and a few points in America. In many regions it appears as a wide-spread endemic,

in others only to a small extent, affecting every age of life, but for the most part between the tenth and twentieth years; cure is very rare. Death generally results from anæmia, atrophy, profuse diarrhœas, pneumonia, pleuritis, or meningitis.

The common form of lepra, LEPRA TUBERCULOSA, is characterized by a nodular formation. There are developed in the skin and in many other organs tumors which by their whole nature belong to the lymph-cell tumors. These vary in size from that of a pea to that of a hazel-nut, sharply circumscribed, at first dense, with a smooth, homogeneous section, but soon they become soft, pap-like, and liquefy, whereby the included tissues are destroyed with them, resulting in the formation of cavities and ulcers; their color is yellowish-white. The microscope shows that the tumors are for the most part composed of round granular cells, like lymph-cells, between which is found a granular albuminous substance. The nodules are at first small, and grow by continuation of the new-formation in the periphery for a long time, until they reach their size and then perish. Sometimes there is a secondary extension to the lymph-glands. Lepra-nodules are developed, under preceding red spots, at first in the skin and in the corium itself, especially of the face, but also of the trunk and extremities. Primarily they always appear multiple: they are at first hard, but they gradually soften, break through the skin and form ulcers, which are for the most part covered with thick crust, in which in Norway numberless itch-mites are found. Sometimes the nodules before breaking through gradually disappear again; in rare cases, in which the ulcers heal, are formed white, radiate, fibrous cicatrices. The nodular formation and ulceration extend also to the eyelids, conjunctiva, the mucous membrane of the mouth, the tongue, the nasal cavities, especially the septum, the mucous membrane of the larynx, trachea and bronchi; then to the mucous membrane of the intestines, uterus and tubes. Numerous nodules are also found in the serous membranes, in the liver, spleen and kidneys, secondarily in cervical, bronchial, mesenteric, and cœliac glands. The lung always remains free (in internal organs the distinction is hereby made from tuberculosis, with which lepra otherwise has great similarity).

In the other form of lepra, LEPRA ANÆSTHETICA, the nodules are absent; on the other hand, there is found on the surface of the spinal cord a thick yellow, dense mass, which acts like a fibrinous or albuminous exudation, but probably represents a diffuse new-formation of the same character as the lepra-nodules. By these masses the spinal cord becomes atrophic, and then there results paralysis of sensation, later also of motion with alteration of nutrition, which is manifested as mummification and necrosis of the skin, gangrene of the fingers and toes and throwing off of these. In some cases lepra tuberculosa and anæsthetica are combined in the same individual.

5. CONNECTIVE-TISSUE CANCER (MEDULLARY CANCER).

Of the two chief forms of cancer new-formation, the epithelial and the connective tissue, the latter should be considered here. But for many reasons both forms of cancer will be considered together, *infra*.

XI. NEW-FORMATION OF CYTOGENIC TISSUE

(ADENOID SUBSTANCE, RETICULAR CONNECTIVE TISSUE).

Consult the works on normal and pathological histology of BILLROTH, HIS, VIRCHOW, HENLE, KÖLLIKER, HEIDENHAIN, FREY, SCHMIDT, ECKHARD, W. MÜLLER, STIEDA, LUSCHKA, KRAUSE, BOLL, ROLLET, RECKLINGHAUSEN, the AUTHOR, as well as the literature of typhous and leucocythæmic new-formation.

CYTOGENIC or ADENOID or RETICULAR CONNECTIVE TISSUE, formely called FALSE or CONGLOBATE GLANDULAR TISSUE, consists of a vascular fibrous framework and of cells. The former forms, about the vessels or independently, net-works of either stellate nuclear or non-nuclear cells, which proceed from the cellular net-work, trabeculæ, affording gelatin or albumen, similar to connective tissue or elastic tissue, which resist acids, but not caustic alkalies. The cells, with little fluid, fill the round or angular meshes of the

framework as dense masses. They resemble the colorless corpuscles of the blood and lymph, or are free nuclei. They increase actively, and so in many places serve as compensation for those which pass out of the affected organs into the lymph and bloodvessels. Cytogenic substance is found in the lymph-glands, in the pulp and Malpighian bodies of the spleen, in the tonsils, in the glands at the root of the tongue and in the pharynx, in the gastric and intestinal follicles, in the mucous membrane of the stomach and intestines, in the thymus, etc. It is sometimes contained in follicles, sometimes in masses and without defined limit in the more common connective tissue.

NEW-FORMATION OF CYTOGENIC SUBSTANCE is of frequent occurrence, in form of hypertrophy, as well as of tumor. The latter is more rarely hyperplastic and then shows numerous transitions to hypertrophy; it is much more often heteroplastic. A regeneration of cytogenic tissue in its entirety is not yet certainly known.

Most of the processes here concerned are not so sharply defined as is the case in new-formation of other tissues, but in part pass into one another, in part into many acute and chronic inflammations and into some new-formations already described, glioma and sarcoma. Besides, our histological knowledge with respect to the new-formations in question is often insufficient to authorize us to establish more sharply defined limits. The mode of origin of cytogenic tissue is not yet known with certainty, and even the derivation of the round cells lying in the spaces of the tissue is not infrequently doubtful: they may proceed from the net-work, or be introduced with the lymph, or have migrated from out of the bloodvessels. Still more imperfect is our physiological knowledge of normal, as well as of the new-formed cytogenic tissue: for while the small round cells formed in many hypertrophies of this kind serve in some cases for the increase of colorless blood-corpuscles (many acute diseases, such as typhoid and puerperal fevers, and especially leucocythæmia), nothing similar is known of most other new-formations, which are the same or similar, macroscopically and microscopically.

On the development of normal cytogenic tissue, see also SERTOLI, *Wien. acad. Sitzgsber.*, LIV., p. 149.

A. HYPERPLASTIC FORMATION, OR TRUE HYPERTROPHY OF CYTOGENIC TISSUE.

HYPERPLASIÆ OF CYTOGENIC TISSUE are frequent, acute or chronic, local or wide-spread. The organs affected increase in various degrees in volume.

Hypertrophy of cytogenic tissue affects either only its soft cellular parts, or all its elements. HYPERTROPHY OF THE CELLS consists sometimes only in their ENLARGEMENT and in an increase of the intercellular fluid (*e.g.*, so-called catarrh of the lymph-glands), sometimes and much more frequently in an INCREASE OF THEIR NUMBER: hyperplasia of the juice. But since the cells of the tissue of the lymph-glands, spleen, etc., are not to be distinguished from colorless blood-corpuscles and pus-corpuscles, they are identical therewith, since also the causes of the hyperplasiæ and inflammations coincide in many respects, so for the most part there remains no limit between the two processes until further processes, especially abscess-formation, make their appearance. Hypertrophy of the vascular fibrous framework rarely occurs alone, but for the most part with increase of cells.

a. Hypertrophy of lymph-glands

is rarely primary, oftener secondary; it is acute, subacute and chronic. The following forms are distinguished:

α. The pure hyperplastic form, in which there results a new-formation of follicles, lymph-channels, and bloodvessels;

β. The hypertrophic form, wherein the follicles, as well as vessels, are enlarged by increase of all their elements;

γ. That form, in which the follicles increase in size, by simple increase of the juice of the lymph-glands;

δ. That form, wherein the trabeculæ and capsule, by infiltration with lymph-cells, are metamorphosed into a tissue like that of the follicular substance, so that the structure of the gland at all points is perfectly uniform.

The first two and last forms are mostly chronic, the latter forms the lympho-sarcoma proper of surgeons; the third form is acute and represents the common non- or half-inflammatory swellings of the lymph-glands.

According to W. MÜLLER (*Z. f. rat. Med.*, CXX., p. 119), all the elements participate in true hyperplasia of the lymph-glands. The sub-capsular, so-called enveloping spaces are retained in part even with considerable enlargement of the glands. The tissue of the lymph-channels shows a preponderating embryonic character, consisting of a granular, striated, pale basis substance containing delicate nuclei, which increase by division. The new-formation of lymph-glands results in such manner that in this embryonic tissue of the lymph-channel, delicate connecting fibres appear between the lymph-glands, which are connected with the offshoots of adjacent capillaries, and are in part transformed into thin-walled capillaries. These vascular connecting fibres, enveloped with lymph-corpuscles which proceed from a part of the embryonal nuclei, become lymph-tubes, in which there later appears the fibrous net-work and a distinct incomplete boundary lamella. Some portions of the fibrous net-work may also persist in the broad lymph-tubes formed in the embryonal state. The ampullæ enlarge by increase of the lymph-bodies and metamorphosis of the fibrous net-work into a nucleus-bearing substance more embryonic in character.

In PRIMARY hypertrophy occurring in external parts (neck, etc.) and in cavities, which occurs in otherwise healthy and in scrofulous, for the most part young individuals, the lymph-glands are similar to many sarcomata, but are distinguished especially by the homogeneousness of the superficial and cut surfaces, by the intimate blending of lymph-gland swellings of other kinds with the neighboring glands. Consult especially BILLROTH, *Beitr.* 1858, p. 168; *Virch. Arch.*, XXI., p. 423.

To SECONDARY hypertrophy of lymph-glands belong most lymph-gland swellings in simple inflammation of peripheric parts, external (inflammations of the skin, psendo-erysipelas, etc.) as well as internal (*e.g.*, bronchial glands in bronchitis, pneumonia, mesenteric glands in intestinal catarrh, cholera, etc.), in many so-called zoonoses, in infection from dead bodies, in many contagious diseases, especially scarlet-fever, small-pox, syphilis, in many pyæmiæ, in typhoid fever (so-called medullary infiltration of the mesenteric, hepatic, splenic, bronchial glands), in leucocythæmia (so-called lymphatic leucocythæmia), in cancer (so-called sympathetic or consensual gland-swelling), etc.

See also HANSEN, *Bidrag til Lymfekertlernes norm. og patol. Anat.*, 1871.

Swelling of the lymph-glands affects sometimes only one or a few adjacent glands of external or internal parts; sometimes a series of them on the surface of the body (simple and syphilitic inflammations, *post mortem* infection, scrofulosis, etc.); sometimes finally most external or most internal lymph-glands, or both at the same time (leucocythæmia, so-called primary hypertrophy without leucocythæmia, etc.). The lymph-glands thus changed exist for a long time without further change, sometimes they continue to grow, sometimes further changes appear in them (inflammation, suppuration, ichorization, tuberculization, calcification, etc.).

b. HYPERTROPHY OF THE SOLITARY FOLLICLES

of the stomach, large and small intestines, as well as of Peyer's patches in the small intestines, occurs, especially in the lower portion of the small intestines, in various degrees and under varying conditions. The latter correspond in general to those processes in which also the mesenteric glands show a like affection. The histological forms resemble those of the lymph-glands.

In typhoid fever this hypertrophy of the intestinal follicles, proper mesenteric glands and spleen, forms the most important anatomical character. But often at the same time here there is found a new-formation of cells and a deposit of them, corresponding to the conditions of cytogenic tissue, into the pre-existing connective tissue, also in the vicinity of the affected portions of the intestines, even into the peritoneum, liver, etc.

According to HENLE, solitary follicles (conglobate glands) sometimes occur also in the vagina.

A probably heteroplastic new-formation of solitary glands in the great omentum is described by WEDL (*Oestr. Jahrb.*, 1861).

c. HYPERTROPHY OF THE SPLEEN

often occurs as such, in form of the so-called swellings of the spleen with increase of the size of the follicles or of the quantity of the pulp or of both at the same time, with or without hyperæmia. The conditions under which these true and false hypertrophies appear, are essentially the same as in hypertrophy of the lymph-glands. The greatest volume is reached by the hypertrophic spleen in lienal leucocythæmia. The microscopical relations of all these forms are known only imperfectly.

ROKITANSKY (*Wien. allg. med. Ztg.*, 1859, p. 98), GRIESINGER (*Arch. d. Heilk.*, V., p. 393) and others found in the interior of the spleen small or larger encapsuled tumors, which consisted of splenic tissue, and which were analogous to the so-called accessory spleens.

d. Most SWELLINGS OF THE TONSILS, not acute, are dependent upon a true HYPERTROPHY of their glandular tissue, for the most part with simultaneous increase of the contents and stroma of the follicles.

In what relation this hypertrophy in children stands to the sometimes simultaneously present emaciation, deformity of the thorax, anæmia and digestive difficulties, it is still unknown.

e. HYPERTROPHY of the cytogenic tissue of the POSTERIOR WALL OF THE PHARYNX not rarely occurs, sometimes diffuse, sometimes in form of tumors varying in size from that of a pea and larger.

B. WAGNER, *Arch. d. Heilk.*, VI., p. 316.

f. HYPERTROPHY of the cytogenic tissue of the CONJUNCTIVA is the condition of the so-called trachoma.

The lymph-follicles of the conjunctiva, which are regarded as pathological forms by STROMEYER (*Deutsche Klinik*, 1859), BLUMBERG, WOLFRING and others, are of a physiological nature (BRUCH, HENLE, KRAUSE, HUGUENIN). (SCHMID, *Lymphfollikel d. Bindehaut des Auges.*, 1871.)

g. So-called hypertrophies of the THYMUS GLAND of the new-born, children and adults, and of various degrees, have been described in quite large

numbers; and yet there is still wanting a pathologico-histological investigation of them.

h. RED BONE-MARROW

consists, according to more recent investigations, of cytogenic tissue, and, histologically as well as functionally, is to be placed by the side of the spleen, partly also by that of the lymph-glands. Histologically, a like character of the medullary elements is found in the bone-marrow, and a similar arrangement and structure of the bloodvessels (the small arteries pass directly into much wider thin-walled blood-spaces, analogous to the cavernous splenic veins). After injection of insoluble coloring matter into the blood, this appears also in the bone-marrow, especially abundant in that of animals whose spleen has been removed (*vide* p. 154). The behavior of bone-marrow varies with the bone, age, etc.: so-called red, lymphoid or lymphatic,—so-called yellow or fatty,—and mucous or gelatinous medulla. The former is found in all fœtal bones, and in those of the child until from the tenth to the fifteenth year. It remains in the bones of the trunk and in those of the cranium, while in the remaining bones fatty medulla appears in its place. The third occurs in senile marasmus and in exhausting diseases in place of the second. The cytogenic tissue principally, in an especially striking manner the bone-marrow, takes a manifold part in the general diseases of the organism. Concerning acute general diseases *vide* p. 440. In chronic diseases with general marasmus it is often transformed into a substance like mucous tissue. The yellow fatty medulla of tubular bones passes, under the same conditions, into cytogenic tissue.

Consult VIRCHOW, *Entw. des Schädelgrundes*, 1857, pp. 36 et al.—RECKLINGHAUSEN, *Canst. Jahr.*, 1867, I., p. 324.—Especially NEUMANN, *Med. Ctrlbl.*, 1868, p. 689; 1869, No. 19.—*Arch. d. Heilk.*, 1869, X., pp. 68 et 220; *Ib.*, 1870, XI., p. 1.—Also BIZZOZERO, *Gaz. med. Lomb.*, 1868, No. 46; 1869, No. 2; *Virch. Arch.*, 1871, LII., p. 56.—HOYER, *Med. Ctrlbl.*, 1869, No. 16 et 17.—PONFICK, *Virch. Arch.*, 1869, XLVIII., p. 1; *Ib.*, 1872. LVI., p. 534.—WALDEYER, *Ib.*, 1871, LII., p. 305.

Since the arterial transition-vessels of bone-marrow have constantly a very much smaller lumen than the capillaries, the circulation in them is a very sluggish one. By this, and in consequence of their special structure, a metamorphosis of the abundantly accumulated colorless blood-corpuscles into colored is favored and actually takes place. Consult especially NEUMANN (l. c.), and the formation of blood-corpuscles. Bone-marrow, like the spleen and mesenteric glands, contains numerous large cells with remarkably numerous red blood-corpuscles, which undergo pigmentary metamorphosis. This is most intense and extensive in typhoid fever, but is also found in less degree in other febrile diseases.

Like NEUMANN, PONFICK also found many pathological changes of bone-marrow, corresponding to known changes in the spleen: the yellow foci from embolism of the nutrient artery, sarcoma, tubercle. Gelatinous metamorphosis, which preponderatingly affects more advanced age, occurs only on the extremities of bones. In acute infectious diseases, especially typhoid, relapsing, intermittent fevers, also pneumonia, there is found, as in the spleen, a strong hyperplasia of all the elements with nuclear growth, and giant-cells (cells containing blood-corpuscles and lymphoid elements). P. also saw an extended fatty change of the vessel wall (not observed in the spleen). In amyloid disease, only insignificant changes are found in the medulla.

Hypertrophies have been observed with certainty, neither in the SUPRA-RENAL CAPSULES, nor in the PITUITARY GLAND.

B. HETEROPLASIA, OR HETEROLOGOUS FORMATION OF CYTOGENIC TISSUE.

New-formation of cytogenic tissue in parts of the body where it does not occur in a normal manner, is found under very varying conditions, as well

with respect to the causes, as the gross and histological structure, as finally the relations to single organs and to the whole organism. It seems proper here to consider together a number of new-formations, which are by others included in connective tissue. Some of these new-formations greatly resemble in their structure the tissue of the lymph-gland follicles, so that their belonging to cytogenic tissue is not to be contested: especially tubercle. The other new-formations contain as the most important element, cells, which resemble colorless blood- and lymph-corpuscles, while the stroma is for the most part common connective tissue poor in vessels (lymphoma proper). Still others have on the whole a similar structure, but form larger masses resembling malignant tumors (many medullary cancers proper).

1. TUBERCLE.

(Tuberculosis and scrofulosis.)

BAYLE, *Rech. sur la phthisie Pulm.*, 1810.—LENNEC, *Traité de l'auscult. méd.*, 1. éd., 1826 ; 2. éd., 1837.—SCHRÖDER V. D. KOLK, *Obs. anat.-path.*, etc., 1825 ; *Nederl. lancet.*, July, 1852.—LOMBARD, *Essai sur les tubercules*, 1827.—CERUTTI, *Coll. quad. de phthisi pulm.*, 1839.—LOUIS, *Rech. anat.-path.*, 1842.—CLESS, *Arch. f. phys. Heilk.*, 1844, III.—ADDISON, *Transact. of the Prov. Med. and Surg. Assoc.*, 1845, II., p. 287. REINHARDT, *Ann. d. Berl. Char.*, 1850, I., p. 362.—VIRCHOW, *Würzb. Verh.*, 1850, I., p. 89; II., p. 24 et 70 ; III., p. 98 ; *Wien. Wochenschr.*, 1856. No. 1 ff. ; *Deutsche Kl.*, 1852, No. 25; *Arch.*, XXXIV., p. 11; *Geschwülste*, 1865, II., p. 620.—LEBERT, *Traité des mal. scroph. et tuberc. (Lehrb. d. Scrophel- u. Tuberkelkrkh.*, Uebers. v. Köhler. 1851); *Bull. de l'acad.*, XXXII., p. 119; *Virch. Arch.*, XL., p. 142 et 532.—BENNETT, *Path. and Treat. of Pulm. Tubercul.*, 1853.—SCHRANT, *Nederl. Weekbl.*, 1854. —KÜSS, *Gaz. méd. de Strasb.*, 1855.—R. HALL, *Brit. Rev.*, 1855 and 1856.—HESCHL, *Prag. Viljschr.*, 1856, III , p. 17.—BUHL, *Ztschr. f. rat. Med.*, 1856, VIII., p. 49; *Lungenentz., Tuberc. u. Schwinds.*, 1872, p. 96.—W. MÜLLER, *Ueb. Struct. u. Entw'ckl. d. Tub. in d. Nieren.*, 1857.—DEMME, *Virch. Arch.*, 1851, XXII., p. 155.—FÖRSTER, *Würzb. med. Ztschr.*, 1861, I., p. 130; III., p. 200.—RINDFLEISCH, *Virch. Arch.*, 1862, XXIV., p. 571.—COLBERG, *Obs. de penit. pulm struct.*, 1863.— HEDINGER, *Die Entw. d. Lehre v. d. Lungenschwindsucht, etc.*, 1864.—VILLEMIN, *Gaz. méd. de Par.*, 1865, No. 50 ; *Gaz. hebd.*, 1866, No. 42-49 ; *Etud. sur la tuber-culose*, 1868.- EMPIS, *De la granulie ou maladie granuleuse*, etc., 1865.—NIEMEYER-OTT, *Klin. Vortr. üb. d. Lungenschw.*, 1866.—HOFFMANN. *Arch. f. klin. Med.*, 1867, III., p. 67.—HÉRARD et CORNIL, *La phthisie pulm.*, 1867.—COLIN, *Bull. de l'acad.*, Aug., Oct.—Dec., 1867 ; Jan.—Aug., 1868.—COHNHEIM, *Virch. Arch.*, 1867, XXXIX., p. 49.—LANGHANS, *Ib.*, XLII., p. 382.—COHNHEIM and FRANKEL, *Ib.*, 1868, XLV., p. 216.—KLEBS, *Ib.*, XLIV., p. 242.—SANDERSON and SIMON, *Med. Times and Gaz.*, 1868, p. 431.—SANDERSON, *Brit. Med. J.*, 1868, No. 381.—W. FOX, *Ib.*, No. 386-388 ; *On the Artif. Prod. of Tubercle in the Lower Anim.*, 1868.—E. WAGNER, *Arch. d. Heilk.*, 1870, XI., p. 497 ; XII., p. 1.—SCHÜPPEL, *Unters. üb. Lymph-drüsentuberc.*, 1871.

The history of tuberculosis reaches much farther back than that of miliary tubercle : HIPPOCRATES describes pulmonary phthisis in a manner worthy of imitation. STARK (1785) and BAILLIE (1794) first described miliary tubercle. LORAIN, ROBIN and EMPIS discovered miliary tubercle a second time ; the latter called it " *granulie ou maladie granuleuse.*" SCHÖNLEIN in the third decade of the present century first used the word *tuberculosis*.

TUBERCLE is an infiltrated or nodular, almost always multiple, round or irregularly formed, for the most part miliary, non-vascular new-formation of varying size, which consists especially of nuclei, small and large, indifferent cells, and giant-cells—all imbedded in a reticular tissue ; it constantly passes, after long duration, into so-called cheesy atrophy, often also into softening ; and appears rarely as a local affection, but most often as a constitutional disease (tuberculosis and scrofulosis).

Circumscribed or nodular tubercles are sometimes visible only micro-scopically (liver, cerebral meninges); most often they are just perceptible (serous membranes, lymph-glands), sometimes they reach the size of a millet seed (so-called MILIARY TUBERCLE, gray, semi-translucent GRANULATION); more rarely are they the size of a pea, cherry, egg and larger (so-called LARGE TUBERCLE, or CONGLOMERATE NODULES: almost only in the brain, testicles, and on serous membranes). Their shape is most often round or rounded, regular or with peripheral serrations; they are rarely flat, but for the most part globular. They may, however, by confluence assume an irregu-lar form and a considerable size: so-called TUBERCULAR INFILTRATION; especially on many mucous membranes (urinary passages, female genitals). Their periphery is apparently sharply defined, but without capsule. Their number is on the whole dependent upon the size: in considerable volume they are usually single or present in small number, while the smallest tubercles occur usually in colossal numbers, are uniformly distributed or arranged in groups of various sizes.

The smallest tubercles are in the fresh state as clear as water or grayish-white, translucent, semi-solid, elastic, moist; their cut surface does not permit, on account of its smallness, of a sufficiently critical examination: FRESH or GRAY TUBERCLE. Large tubercle as well as tubercular infiltra-tions show peripherically on section almost always a similar, regular or irregular, grayish-white, translucent, homogeneous, non-vascular, moist zone of varying breadth; the larger central portion, on the other hand, is almost always grayish-yellow or yellow, opaque, dry, inelastic, and of cheesy con-sistence: so-called YELLOW TUBERCLE.

MICROSCOPICALLY, fresh miliary tubercle consists, in proportion to its size, of one or many (for the most part 4–6, more rarely 12) rounded, sharply defined NODULES or FOLLICLES, whose diameter reaches 0.35–0.15 mm. Each follicle is composed of a reticulum, in the spaces of which are cellular elements: hence the name CYTOGENIC or RETICULAR TUBERCLE.

The RETICULUM is, in general, like that which occurs at various ages in normal reticular connective substance, except that it is usually somewhat broader: it consists sometimes of distinct or indistinct, many-branched nucleated cells, sometimes of a smaller or broader, fibrous substance with elongated nuclei. In the periphery there is sometimes found a lighter space, similar to the so-called enveloping space of the lymph-gland follicles with fine elastic fibres. The periphery more often shows broader, denser, nucleated fibres, the course of which is nearly circular, and which form a kind of girdle around the whole tubercle. The reticulum is WITHOUT BLOODVESSELS, and probably without lymphatics. In the youngest tubercles it is very scanty and very soft.

The CELLULAR ELEMENTS of tubercle are free nuclei and small round cells, which are not infrequently also somewhat larger, and sometimes angular. The nuclei are for the most part round, rarely oval, with a diameter of 0.005–0.003, even 0.001 mm.; they are clear, vesicular, with or without nucleoli. The CELLS are most often similar to the colorless blood-corpuscles, for the most part smaller, with 1–2 nuclei; they occur with the nuclei or as the only elements. (According to many, tubercle con-sists only of cells, but which are so frail, that during the investigation most are destroyed, leaving the nuclei.) There are also constantly seen, mostly in the centre, rarely in the periphery of the follicle, one or many so-called POLYNUCLEAR GIANT-CELLS. These vary in size, to that of 0.04 mm., are rounded or elongated, dark granular, and many-branched, with for the most part very numerous (to 20, 50, 100 and more), rounded or oval, compara-

tively large nuclei. (See p. 359.) Cells are likewise constantly found, which are intermediate between the small common and the smallest giant cells : they are epithelial-like, rounded, finely granular, with one large or many smaller nuclei.

Tubercle always occupies the place of the normal tissue, which has usually to a great degree wasted away, or, as more rarely happens, is only pushed to one side. The limiting tissue is besides sometimes in various ways changed, sometimes not.

The histology, just given, of tubercle of the most different organs is by the author. Schüppel determined it in a special manner, with respect to the lymph-glands, and indeed with respect to tuberculosis as well as scrofulosis of these. Similar views with respect to the structure of tubercle are held by Virchow, Buhl and Köster (*Virch. Arch.*, XLVIII., p. 95), and with respect to inoculation of tubercle by W. Fox and Sanderson. That giant-cells form an almost constant element of tubercle of most organs, has been shown especially by Langhans.

Fibrous tubercle, according to many, is a peculiar form of tubercle, according to others, only a metamorphosis of it.

Virchow, to distinguish fibrous from common cellular tubercles, designates as the former those which, except in the centre, consist of abundant connective tissue : they occur especially in solid, fibrous parts, and in new-formed connective tissue masses ; they are characterized by their hardness, greater translucence, pearly, light gray appearance. Langhans found the common cellular tubercle chiefly in serous membranes, pia mater, etc., fibrous tubercle more in the lungs, liver, spleen, kidneys, etc. According to L. fibrous tubercle is not destroyed directly, but there is formed within the cellular zone a connective tissue relatively poor in cells, which first is destroyed by degeneration. It is consequently a more highly developed form of cellular tubercle. According to Schüppel, fibrous is a metamorphosis of common tubercle : at least in the lymph-glands the peripheral trabeculæ of the reticulum and the adjacent trabeculæ of the glandular reticulum are metamorphosed into homogeneous or indistinctly striated connective tissue. The centre of the tubercle at the same time undergoes cheesy transformation.

Microscopical examination of the OLDER, so-called yellow, as well as of the centre of most fresh TUBERCLES shows CONSTANT SIMPLE ATROPHY, or NECROSIS of the nuclei and cells above mentioned, and also of the reticulum, often also FATTY METAMORPHOSIS of less degree. Through the former atrophy, first the nuclei and round cells, latest the giant-cells are metamorphosed into irregularly formed, for the most part smaller, flat, homogeneous or furrowed, dull, very soft corpuscles (so-called tubercular corpuscles), and finally into a finely granular detritus. These atrophic elements, some cells which have suffered partial fatty degeneration, simple and fatty detritus, form the only elements of yellow tubercle. Sometimes the surrounding compressed tissues undergo the same change. In many cases the denser peripheral zone becomes hypertrophic : its fibres thicken, the intervening cells and nuclei become indistinct ; the whole finally resembles common cicatricial tissue. Atrophy of tubercle is the consequence of its insufficient nutrition through the vessels around it. At what age of the tubercle this change appears, has not been determined ; for the most part a few weeks appear to suffice to call it forth, at least in the centre of the tubercle, while at other times months are necessary.

Simple atrophy of tubercle-elements occurs so often, even in the centre of apparently fresh tubercles, that the so-called TUBERCLE-CORPUSCLES OF LEBERT and the yellow and cheesy character of the tubercle proceeding from that atrophy, were a long time regarded as their most essential property. But since the structure of

tubercle has been learned more accurately, and the same metamorphosis has been found in cell-accumulations of every kind, it is no longer characteristic. But the name TUBERCULIZATION has been retained. (See p. 297.)

FRESH MILIARY TUBERCLE ONLY IS CHARACTERISTIC, macroscopically as well as microscopically. If simple atrophy of the whole tubercle has already appeared, a distinction between it and many inflammatory affections connected with suppuration, and many syphilitic, sarcomatous, and carcinomatous new-formations—if in these a like extensive atrophy is present—is more difficult, but for the most part still possible. This is true especially of the larger so-called tuberculous infiltrations of the mucous membranes, of the older tubercles of lymph-glands and of the large tubercular nodules of the brain. In the lungs the appearance of the older miliary tubercles with grayish-white periphery and yellow centre is formed sometimes by transverse section of the small bronchi, the lumina of which are filled with cheesy pus, and the walls of which are thickened.

CORNIFICATION is that condition of miliary tubercle which is effected by simple atrophy of the nuclei alone (without simultaneous fatty metamorphosis): the tubercle is transformed into a hard, horny mass.

The FURTHER CHANGES OF TUBERCLE, after a longer duration of simple atrophy and fatty metamorphosis, are the following:

RESORPTION, which is accomplished by simple, but especially by fatty atrophy, occurs most rarely; it is complete only in the smallest tubercles, in the larger it is followed for the most part only by their diminution.

CALCIFICATION, more rarely alone, for the most simultaneously with cheesy atrophy, affects large and small tubercles : if it occurs alone, the tubercles are transformed into stony masses; if fatty metamorphosis is present at the same time, there arises a grayish-yellow greasy soft mass, with here and there greater consistence. In rare cases the chalky masses are laminated.

SOFTENING or LIQUEFACTION, the most important and most frequent change, occurs through unknown chemical metamorphoses, rarely in the smallest, more often in the large yellow tubercles. Upon this, with cheesy metamorphosis at the same time, depends, according as it affects mucous membranes or parenchymata, the TUBERCULOUS ULCER, or TUBERCULOUS CAVITIES (tuberculous abscess). Both rarely occur pure, not complicated with suppuration; more often the latter follows, especially after throwing off of all tuberculous matter. The ulcer occurs especially on the mucous membrane of the intestinal canal and air-passages, more rarely on that of the urinary and sexual organs, and bile-ducts, on serous and synovial membranes : cavities in the lungs, lymph-glands, in the brain, testicles, prostate, supra-renal capsules, etc.

TUBERCULOUS ULCER is in the beginning small, round, crater-like, infiltrated in its base and walls by tuberculous matter : so-called PRIMARY ULCER. In its further course it grows either circularly and unites with neighboring ulcers; or especially in one direction, e.g., in the intestines tranversely to the direction of the villi : so-called SECONDARY ULCER. At other times, from the beginning in an extensive tuberculous infiltration, and with its softening and destruction there is formed a large tuberculous ulcer, the base and walls of which still contain abundant yellow tubercular masses (vermiform process, uterus, urinary passages). The small as well as large ulcers may progress from the mucous membrane into the sub-mucous tissue, and from there into the muscular and serous coats.

TUBERCULOUS CAVITIES are represented by for the most part rounded cavities, of varying size, which are filled by a thin purulent, or cheesy purulent liquid, often at the same time with yellowish crumbling masses, and are infiltrated to a varying thickness with tuberculous matter. They may penetrate into surrounding cavities (pleura) or to the external surface of the body (tuberculous fistula of the epididymis). The so-called tuberculous cavities of the lungs have their origin, to a small extent, in tuberculosis of the small bronchi and of the surrounding pulmonary vesicles; to a

larger extent, they are sacculated bronchicctases, the inner surface of which is gener-
ally, or at points ulcerated or tuberculous.

HEALING OF TUBERCULOUS ULCERS AND CAVITIES occurs extremely rarely.   It
occurs through evacuation of the softened tubercle and a secondary new-formation
of connective tissue, and is followed for the most part by contraction of the affected
mucous membrane.   ENCAPSULING of tubercle consists in the formation of a
connective tissue envelope around the tubercle ; the latter therein always undergoes
cheesy degeneration ; it is not infrequently calcified.

The ORIGIN OF TUBERCLE is in connective tissue of different kinds :
especially that of the so-called lymph-sheaths of small arteries, lymphatics,
perhaps also of small veins; also the tissue of serous membranes.   In
all these parts tubercle probably proceeds from a growth of the common
so-called fixed connective-tissue corpuscles and the endothelium identical
therewith.   Whether tubercle can arise also from the endothelial layer of
serous membranes, blood- and lymph-vessels, is still doubtful.   The more
intimate microscopic relations of the origin of tubercle are not yet
accurately known.   (Tubercle, in spite of its cytogenic structure, proceeds
not from the cytogenic tissue of organs which contain it, e.g., intestinal
mucous membrane.)

The origin of tubercle has been pursued especially in the fresh miliary
tubercles of serous membranes and of the pia mater of the brain, in the
liver and kidneys.   Here tubercle is developed by repeated division of
the connective tissue corpuscles or by endogenous formation ; the connec-
tive-tissue basis substance, epithelial and gland-cells, and capillaries are
more or less—the latter perfectly—destroyed by the immense nuclear
formation.   In other tissues, also the lungs, as well as in connective tissue,
tubercle arises partly by manifold division of the nuclei of the capillaries,
partly by simple division of the nuclei of the adventitia of the larger and
smaller vessels, of the sarcolemma, so-called structureless sacs.   The reti-
culum of tubercle is partly the original lost connective tissue, only pressed
apart, and of the higher elements (gland-cells, vessels, etc.), which perhaps
have also become somewhat hypertrophic; it is partly new-formed.   (Con-
sult the following numerous, but still very differing statements.)

HESCHL first demonstrated the formation of tubercle in the lungs, in the wall of
the capillaries ; as well as of other vessels of every size.   According to VIRCHOW
and BUHL, fresh miliary tubercle is seen in the peritoneum and pia mater along the
finer arteries as vesicular swellings, filled with nuclei, of their adventitia.   The same
was found by ROKITANSKY, WEDL, DEMME, COLBERG, FÖRSTER and others.
According to DEICHLER (Beitr. z. Histol. des Lungengewebes, 1861) the vessel-walls
in the lungs are loosened as far as the intima by new-formed cells, and with the accu-
mulation of cells, separate farther and farther, until finally they are entirely lost in
the larger nodules and the vessels are bounded only by the very thin intima.   In the
pia mater and brain the tubercles, according to RINDFLEISCH, appear like lateral
projections, single or united into small groups on the larger branches, while on the
finer branches and the almost capillary vessels they form spindle-shaped varicosities,
which wholly surrounded the vessels.   According to KLEBS (Virch. Arch., XLIV.,
p. 256), a larger part of the yellow and gray knots, which are met with on the base of
tuberculous ulcers, are situated in the lumen of the lymph-vessels.   Rows of nodules
in the course of the lymphatics, often as far as the nearest glands, are seen in tuber-
culous ulcers of the intestines (Lymphangoïtis tuberculosa).   Similar statements
are made by RINDFLEISCH and KUNDRAT.   AUFRECHT (Med. Ctrlbl., 1868, No. 28)
regards miliary tuberculosis of the peritoneum as a granular peri-lymphangoïtis.
According to BASTIAN (Edinb. Med. J., 1867, XII., p. 815), miliary tubercles of the
brain arise from the endothelium of the lymph-sheaths, in which the cerebral vessels
lie.   According to SANDERSON, miliary granulations on the diaphragm are situated
in the course of the veins, not of the lymphatic vessels.   According to ARMAUER-
HANSEN (Beitr. z. Anat. d. Lymphdr., 1871), tubercles of the serous tunic of the

intestines and of the mesentery are situated on the exterior of the lymphatic vessels (in opposition to LANGHANS and KLEBS). Also in the intestinal tube they are situated in the follicles or in the sub-serous tunic outside of the sinus and vessels. The myeloplaxes arise from lymph-cells, not from the endothelium of the lymphatic vessels. In the bronchial glands they are not infrequently pigmented. According to BUHL (*Lungenentz.* etc., p. 106) the alveolar epithelium of the lungs is itself the seat of tubercular new-formation; it extends from the interior wall of the alveoli into the textureless lymphatic vessels. See also RANVIER (*Nouv. dict.*, etc.)

Tubercles of the choroid arise, according to COHNHEIM, from the contractile WANDERING CELLS of this membrane. BILLROTH's latest view of tubercle-cells generally is similar to this. According to SCHÜPPEL (*Arch. d. Heilk.*, 1868, IX., p. 524), numerous tubercles of the liver are formed in an EMBOLIC manner on the interior of the bloodvessels, with participation of the connective-tissue bodies and capillary nuclei, only by metamorphosis and growth of the colorless blood-corpuscles WITHIN the bloodvessels themselves. The mother-cells with manifold nuclei distend the capillaries, leading to atrophy of the liver-cells, and then represent the tubercular nodules.

According to SCHÜPPEL (l. c., 1871), tubercle of the lymph-glands arises in the proper gland-substance (follicles, etc.), not in the septa. The development of tubercle begins, according to SCH., with the appearance of a giant-cell. The latter is often formed, probably for the most part within the bloodvessels, at other times perhaps within the lymphatic vessels.—See also SCHÜPPEL, *Arch. d. Heilk.*, 1872, XIII., p. 69.

In the intestinal canal, my own investigations show that tubercle is developed altogether independently of the solitary follicles and the follicles of Peyer's patches.

According to BUHL (*Lungenentz.*, etc., p. 103), the reticulum proper of tubercle has its origin in a mass analogous to connective substance, which is secreted by the giant- and epithelial cells at the periphery, and which afterward hardens; only the border zone becomes a fibrous organic connective tissue.

The origin of tubercle from epithelial and gland-cells only, as in the liver, kidneys and testicles, has not been demonstrated. Those cells, as well as the epithelium of the lungs and the cells of the lymph-glands, grow, however, sometimes increase in number, or pus-corpuscles are found in their place: both kinds of cells often become cheesy with the tubercle-cells themselves (lymph-glands, kidneys, testicles, lungs).

The GROWTH OF TUBERCLE results, to a small extent, from division of new-formed nuclei. In the vicinity of the largest portion, for the most part with moderate (active or passive) hyperæmia there is the same new-formation of nuclei from the normal tissue, with consecutive destruction of the latter, as in the first origin of it. By the progressive growth of many small tubercles in this manner, these become confluent and result in the formation of many knots varying in size to that of a walnut and larger, as well as in so called infiltrated tuberculous tumors of many mucous membranes (of the urinary passages, Fallopian tubes, etc.)

The FURTHER EXTENSION OF TUBERCLE is sometimes along the connective tissue, in which it first had its origin; sometimes in the course of the lymphatic vessels (this is shown especially in the passage of tubercle from mucous membranes or parenchymata to the corresponding serous membrane); sometimes finally in that of the bloodvessels (regular occurrence of hepatic tubercles in tuberculosis of the intestines).

TISSUES SURROUNDING TUBERCLES are for the most part compressed, and afford especially in older tubercles a series of changes, which sometimes afford only an apparent enlargement of the tubercle, sometimes they truly represent other processes. These changes may hereby become of almost equal clinical importance with the tubercles themselves. They are dependent upon the quick formation of the tubercle, upon the obliteration of the vessels, upon the continuance of the cell-growth on the sheath of the sur-

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rounding bloodvessels, upon the frequently accompanying collateral hyper-
æmia, and hypertrophy of the surrounding tissues, and upon the retrograde
metamorphoses of the tubercle.   Especially worthy of note are :

New-formation of vascular connective tissue, especially in chronic tuber-
cle-formation : it is followed by thickening and the formation of pseudo-
membranes or serous membranes, thickening of the interstitial connective
tissue of the lungs, intestines, glands, etc. ;

Formation of serous, sero-purulent, muco-purulent and purely purulent,
more rarely of croupous and diphtheritic exudations with or without dis-
tinct hyperæmia : on serous membranes, mucous membranes, etc.   In the
lung-tissue, the tissues inclosed by tubercle, as well as those surrounding
them, especially the alveoli, often the finest extremities of the bronchi, are
found filled with epithelial cells, which often show fatty metamorphosis, as
well as with abundant pus-corpuscles and often with molecular fibrin.   A
similar disposition is found in the lymph-glands.   Simultaneously with
simple atrophy of tubercle-elements, pus-corpuscles also undergo the same
atrophy as well as fatty metamorphosis.   Thereby there are formed most
larger yellow tubercles and, by their destruction, cavities ; destruction of
bloodvessels with consecutive pigment-formation, destruction of lymphatic
vessels etc.   The former depends upon the enormous new-formation of
nuclei around the capillaries, as well as upon the increase of nuclei, which
takes place in the wall of the vessel itself.

In tuberculous destruction as well as in numerous tuberculous cavities of the lungs
there are early formed anastomoses between the region of the pulmonary artery and
that of the bronchial artery, after attachment of the pleura also with the intercostal,
mammary and phrenic arteries.   Thereby is an excessive congestion of blood in the
air-breathing portions of the lungs prevented (SCHRÖDER V. D. KOLK, GUILLOT).

TUBERCULOUS INFLAMMATIONS, so-called, of organs arise through COMBI-
NATION OF TUBERCULOSIS WITH INFLAMMATION.   Inflammation in such cases
is characterized by new-formation of vascular connective tissue, which is
met with either in the stage of granulation-tissue rich in cells, or which is
poor in cells and of older date.   There lie imbedded therein tubercles of
microscopic size, which reaches that of a pea and larger ; in the former
case they are fresh and gray, in the latter case older and yellow.   Tuber-
culous inflammations are purest, and most easily recognizable in serous
membranes, also in the joints (many forms of so-called *tumor albus*).   They
are less pure on many mucous membranes (most so-called primary tubercu-
lous formations of the calices and pelvis of the kidneys, of the uterus with
the Fallopian tubes, perhaps also many of the larynx, trachea and bronchi).
They are least pure in parenchymata, most often in the testicles and
lymph-glands, according to many, also as the cheesy tuberculous knots in
the brain, spleen, bones.   The clinical form is sometimes more that of sub-
acute or chronic inflammation (serous and many mucous membranes),
sometimes more that of tuberculosis (testicles, lymph-glands, brain), some-
times it is mixed.   Hence it follows, that in many of the localities named
the boundary line between tuberculous inflammation and chronic tubercu-
lar knots and tubercular infiltration cannot be drawn.

BUHL (l. c., p. 132) has more recently brought prominently forward the peculiari-
ties of tuberculous inflammations.   According to B. (l. c., p. 68) the so-called cheesy
or tuberculizing pneumonia proceeds neither from catarrhal nor from croupous, but
from the pneumonia described by him as parenchymatous or desquamative.   This is
characterized by new-formation of nuclei and cells in the inter-alveolar tissue, in the
adventitia of vessels and in the external layer of the small bronchi and bronchioles

on the one hand, by desquamated and increased pulmonary epithelium on the other hand : both elements undergo cheesy metamorphosis. Cheesy knots of the brain or tuberculous encephalitis arise, according to B., through increase of the endo- and perithelial cells of the arterial vascular sheaths, embryonic new-formation of connective tissue and softening of the interjacent brain-tissue, with consecutive capillary anaemia and necrosis.

Tubercles occur at every age, most often in the young, in both sexes and under every condition. They have not yet with certainty been observed in the fœtus.

The young born of animals inoculated with tubercle, as well as the embryos of such, have never, even during miliary tuberculosis of the mother, shown tubercle.

With respect to its SEAT in individual organs, tubercle shows a varying frequency according to the age of the sick person. In CHILDREN it occurs most often in lymph glands (external, bronchial, and mesenteric glands), lungs, brain, spleen, liver, intestinal mucous membrane, serous membranes and bones. In ADULTS it is found as a PRIMARY affection by far the most often in the lungs ; more rarely in the lymph-glands, urinary organs, genitals, intestinal canal. SECONDARILY, it occurs in almost all organs : chiefly in the lymph-glands, corresponding to the seat of the primary tubercle ; on the intestinal mucous membrane, respiratory mucous membrane, in the liver, spleen, kidneys and supra-renal capsules, the pia mater of the brain, choroid, bone-marrow, etc., in primary pulmonary tuberculosis. Tubercle has never been seen in cartilage, in the external muscles, and in the great vessels ; very rarely in the pharynx, tonsils, œsophagus, vagina, ovaries, heart and tongue, salivary glands, thyroid glands, skin. Primary tubercle of the gastric mucous membrane, of the respiratory mucous membrane, liver, spleen, etc., likewise never occurs or is extraordinarily rare. Not infrequently tubercle is finally developed in many new-formations, especially in pseudo-membranes of serous membranes. Sometimes there occurs an acute or sub-acute tuberculosis (and usually at the same time inflammation with sero-fibrinous exudation) of one, rarely of many serous or synovial membranes ; most often in the pericardium, more rarely in the pleura, and joints, especially the knee-joints. (See Tuberculous Inflammation.)

The smallest miliary tubercles are not visible to the naked eye ; especially on this account have the not infrequently occurring tubercles of the liver, spleen and lymph-glands so long been overlooked. The frequency of the former has for a long time been shown by the author, that of the latter by SCHÜPPEL. According to S. not only the long-known so-called scrofulous gland-tumors belong here, but also the chronic so-called lymph-gland hypertrophies or lymph-gland sarcomata, which are not rare especially on the neck of young persons : the latter are hypertrophies with miliary tubercles.

In some organs tubercles are found distributed at various points in varying number, sometimes quite uniformly over the whole organ. The favorite seat in the lungs is the upper lobes ; in the pia mater, the region between the chiasma and the medulla oblongata ; in the intestinal canal, the ileum and cœcum ; on the respiratory mucous membrane, the posterior and superior surface of the larynx and the small bronchi ; in the bones the spongy tissue ; in the male genitals, the corpus Highmori, the head of the epididymis and the gland-lobules of the testicles ; in the female, the body of the uterus and the Fallopian tubes ; in the kidneys, sometimes the cortical portion, sometimes the pyramids, calices and pelvis, etc.

Tubercles of the choroid, first discovered by MANZ, and more accurately described by COHNHEIM, have recently, by means of the ophthalmoscope, been made use of for the more accurate diagnosis of general acute miliary tuberculosis. They are found especially in the posterior section of the eye, in the vicinity of the optic nerve and macula lutea ; they are regularly rounded, but of very varying size ; the

larger are distinctly prominent. (GRÆFE and LEBER, *Arch. f. Ophthalmol.*, 1868, XIV., 1. Abth., p. 183.)

LAZARUS (*Berl. Diss.*, 1872) describes six cases of disseminate miliary tuberculosis in bone-marrow, in each case with intense tuberculosis of the spleen and lymph-glands.

BIESIADECKI (*Wien. med. Sitzgsber.*, 1868, LVII., p. 788) has four times found tubercle in the larger blood-coagula of serous membranes. In each case the adjacent serous membrane was densely occupied with fresh tubercles ; the extravasated blood always came from the vessels of young pseudo-membranes (*Arch. d. Heilk.*, XI., p. 497.)

The ORIGIN of SECONDARY TUBERCLE is explained sometimes by the manner of spreading by the lymph- and bloodvessels, sometimes it is unexplained. Especially is this true of the so frequent tuberculosis of the mucous membrane of the great air-passages and intestinal canal : in these cases there follows perhaps a direct taking up by the epithelium of the mucous membrane. Certainly many so-called tuberculous intestinal ulcers are of a catarrhal or lardaceous nature.

Tubercular disease is ACUTE, SUBACUTE, or CHRONIC. In all these cases the tuberculosis is either truly primary, or, according to the more recent views, it follows a chronic so-called cheesy inflammation of the same or of another organ. In acute tuberculosis, within a few days or weeks, numberless, for the most part extremely small tubercles (hence acute miliary tuberculosis) are new-formed, in one or many organs, especially in the lungs, serous membranes, pia mater of the brain, liver, spleen and kidneys. In subacute and chronic tuberculosis the first new-formations are formed insensibly, especially in some organs. After weeks, months, years, new tubercles appear in the same or in other organs, until finally through succeeding disease, or through acute tubercle-formation death results.

The INFLUENCE of tubercle on the affected organ consists in the destruction of the tissues at the place of the tubercle, which, especially with respect of size, number, and seat of each, is important, as well in compression or filling out of former hollow-spaces (especially in glandular organs and the lungs) ; in the collateral hyperæmia in the vicinity of the tubercle (hereby arise in the brain softening, in the lungs inflammation of the lung-tissue itself, of the bronchi, in the intestine catarrh, etc.) ; in the hyperæmia and inflammation of the surrounding parts, of the adjacent serous and vascular membranes, etc., accompanying tubercle-formation ; in the processes dependent upon tubercular metamorphosis: narrowing of cavities, *e.g.*, of the intestine ; formation of so-called ulcers and cavities ; perforation of membranes, especially serous and mucous membranes, of vessels in softening of tubercle (thus arise inflammations of serous membranes, hæmorrhages).

The INFLUENCE of tubercle ON THE WHOLE ORGANISM depends : upon the above-mentioned organic disturbances (disturbed respiration, etc.) : upon the fever often accompanying the development of primary or secondary tubercle ; upon the diseases consequent to tuberculosis (besides those above-mentioned easily explained, especially : thrombosis of veins, lardaceous degeneration of the abdominal organs, fatty heart, renal diseases, etc.).

The CAUSES OF TUBERCLE-FORMATION AND OF TUBERCULOSIS are rarely of a LOCAL, but for the most part of a GENERAL nature, and in both cases predisposing and exciting.

Certain LOCAL conditions give rise to tuberculosis, especially at first of the respiratory organs, in those perfectly healthy and in no manner disposed to it. In many trades they produce, through inhaled injurious substances, bronchitis, pneumonia or tuberculosis. Or the respiratory organs are injuriously affected in various ways by excessive, or unilateral, or too

little exercise of them. Foreign substances in the respiratory organs, especially strong mechanical irritants, are direct causes of tuberculosis, while particles coming through the alveoli into the connective tissue from the beginning lead to an increase of nuclei, etc., which become transformed into miliary tubercle. But the secondary effect of these substances on the origin of tuberculosis is certain : either when they cause inflammations and suppurations, which finally become cheesy and are later resorbed ; or when they enter the blood or lymphatic vessels and again passing out of their wall are the conditions of like growths.

In an altogether similar manner perhaps those substances act, which have their origin in the body itself, but in various ways reach the air-passages and the alveoli of the lungs : e.g., catarrhal and other secretions in chronic affections of the nose and pharynx (especially syphilis), in chronic affections of the larynx, perhaps blood in hæmorrhages in the air-passages with aspiration of the blood.

According to HIRT (l. c.) 80 per ct. of those workmen who incur diseases through inhalation of dust, suffer from phthisis : especially file-cutters, goldsmiths, workers in bronze, stone-cutters, polishers of steel and brass, grinders of glass, porcelain, etc.

The GENERAL causes of tuberculosis are partly those which have been acquired by inheritance, partly those which are due to unfavorable external circumstances. HEREDITARY DISPOSITION to tuberculosis shows either no striking characteristics of construction of the thorax, etc. ; or there is found a weak organism, wasted muscles, a narrow thorax, increased irritability of the nerves, and above all a feeble resistance of the organism. In both cases slight exciting causes of all kinds induce with comparative ease tuberculizing inflammations, or directly tubercles themselves. In a second rank, stand INSUFFICIENT NOURISHMENT, insufficient dwellings, etc., in the broadest sense.

Of the GENERAL causes, with reference to heredity, the influence of parentage on the origin of tuberculosis of children is without a doubt often to be determined. Tuberculosis affects children, if both parents or only one of them, especially the mother, are tuberculous. More rarely it affects hereditarily the second generation, while the first remains free from it. Likewise bad nourishment is certainly a frequent cause of tuberculosis. This we see in the unsuitable nourishment especially of small children, also in prisoners, the inmates of orphan asylums, etc. ; in preceding exhausting states, in chronic and acute diseases (long quiet, venereal excesses, grief —large watery evacuations, round gastric ulcer, diabetes insipidus and especially mellitus, constitutional syphilis, cancer of the œsophagus ; typhoid fever, acute exanthemata) ; in insane persons, who refuse food. BIRCH-HIRSCHFELD (Arch. d. Heilk., 1871, p. 501) describes two cases in which extended miliary tuberculosis was developed immediately after typhoid fever. TRAUBE's experiments teach that rabbits which have lived a long time without a supply of water, show always exquisite cheesy inflammations of the lungs.

Tuberculosis is rarely found in those affected by hump-back, emphysema, or diseases of the heart. LEBERT (Berl. klin. Wchschr., 1867, No. 22 ff.) gives prominence to the influence of stenosis of the conus arteriosus, of the pulmonary orifice, and of the pulmonary artery, upon the origin of tuberculosis.

The most northern points of the earth have a certain immunity from consumption, while the tropics show the most considerable prevalence and greatest rapidity in its course (HIRSCH, Hist.-geogr. Path., II., p. 2, etc.). An elevation 2,000 feet above the sea may be regarded as the limit of the occurrence of consumption. On the islands of the Baltic and North Seas (Iceland, the southern shores of Wight) tuberculosis is very rare, while those of the hot zones afford no immunity. Tuberculosis is rare in malarial regions.

Consumption stands in direct ratio to the density of the population : hence its frequency in cities and certain quarters of cities, in closed spaces preventing a change of air (small dwellings, work-rooms, barracks).

The EXCITING CAUSES of tuberculosis are known almost only with respect to pulmonary tuberculosis. They consist in frequently repeated irritations and inflammations of the respiratory organs; in rude changes of temperature (cold); in increased moisture of the air (the places free from consumption are remarkably dry); in a continued residence upon clayey ground and low regions, also in great moisture of the soil (on porous ground and in elevated regions tuberculosis is rare).

According to the older and more recent views, miliary tuberculosis is a SPECIFIC RESORPTION- and INFECTIOUS DISEASE. This is confirmed by the following propositions:

The basis for the development of miliary tuberculosis is a CHEESY FOCUS. Elements taken up out of such into the blood and lymphatic vessels give rise to the multiple development of tubercles (SELF-INFECTION). In by far the greater number of cases one or many cheesy foci are found in the body. The cheesy focus, which leads to miliary tuberculosis, owes its origin to former inflammatory states. Cheesy foci are most frequent in connective tissue, in previously inflammatorily irritated (so-called scrofulous) external and internal lymph-glands, in bones (especially the bodies of the vertebræ and extremities of joints), in the testicles, in the mucous membrane of the uterus, Fallopian tubes, intestines, in the brain, cheesy-purulent exudations of serous membranes, cheesy pneumonia, etc. The infectious material of cheesy foci, upon which tuberculosis follows, contains something SPECIFIC. The cheesy focus may be incompletely encapsuled, not bounded on all sides by solid fibroid tissue. The encapsuling is not an absolute, but a considerable obstacle to resorption. The infection of neighboring tissues is an important proof of the origin of miliary tubercle by resorption. It takes place probably through the lymphatic vessels or plasmatic canals. This infection of neighboring tissues consists in this, that tubercles in the largest accumulations always appear in the immediate vicinity of the infecting focus, and spread thence by intervals in excentric lines. Proofs are most frequently afforded by miliary tubercle about old intestinal ulcers, more rarely those in the vicinity of cheesy carious vertebræ, cheesy bronchial glands, etc. While in certain cases only this infection arises, in others there appears a general infection. The latter consists in this, that similarly large and fresh miliary tubercles are found in many or almost all organs and tissues at the same time. This general infection is most frequent under 24 years of age, i.e.. during the growth of the body, during more active lymph- and blood-formation. In three-fifths of the cases, where a cheesy focus has not been found, the patients affected were old. A further proof is the seat of the tubercle in lymphatic-bearing connective tissue of organs, the analogies of their structure with that of the normal lymphoid organs of the body, even in the physiological condition which calls it into life. Tuberculosis has as an infectious disease its analogies in miliary carcinosis. It is probably transmissible from one human individual to another, like glanders, syphilis. It as a rule is not found together with other infectious diseases (cancer, typhoid fever, pyæmia).

The former was shown by ROKITANSKY, the latter by BILLROTH and MENZEL (Arch. f. klin. Chir., XII., p. 365) empirically, or statistically.

The most striking proof that tuberculosis in a disease of resorption, is the result of inoculation, the transmissibility of tuberculosis to animals.

LAENNEC first distinguished primary and secondary tuberculosis: the latter appears only after softening of the former, and in consequence of peculiar chemical changes. DITTRICH (MARTIUS, Die Combinationserkh., etc., 1853) held the origin of tuberculosis to be through taking up of detritus of retrogressively metamorphosed

normal or pathological tissues. BUHL regards miliary tuberculosis as a specific disease of resorption or infection. The above statements are from BUHL's most recent work (p. 111). The virulent matter, according to BUHL, passes over with the semen to ovum and so become hereditable. From the analogy of infectious matters, only a minimum of tubercular matter is necessary to generate the specific disease, and in every retrograde formation of tissues and exudations there is a stage in which the signs characterizing yellow tubercle are present. For when, at the time of the autopsy, an old focus has not been found with acute miliary tuberculosis, the former may have disappeared by resorption. HOFFMANN saw cheesy inflammations leading to tuberculosis not only in the lungs, but also in other organs, especially in the urinary and sexual organs ; also he lays the chief weight on the accumulation of cheesy masses of detritus in the body as an ætiological factor of miliary tuberculosis. Also in experiments by inoculation, the local inoculated focus was more often found to have disappeared, although the internal organs showed acute tuberculosis. Numerous records of autopsies have more recently been published, which show the origin of miliary tuberculosis from cheesy foci. BUHL, in two groups of 84 and 300 cases, could not find a cheesy focus in 8.2 p. ct. of the former, nor in 10 p. ct. of the latter. H. WEBER (*Transact. of the Path. Soc. of London*, 1869–70) found cheesy foci in sixteen cases of tuberculosis of the meninges or serous membranes. But in many of these publications, not infrequently has the cheesy focus been at once assumed to be an old inflammation-focus. And indeed in the lungs, from my own experience, in the lymph-glands according to SCHÜPPEL's investigations, there may often be shown a cytogenic or tuberculous structure, where, in accordance with the views especially of REINHARDT, and again prevailing but a short time since, a simple cheesy pus-focus should have pre-existed.

RINDFLEISCH (*Nierrhein. Ges. f. Nat.- u. Heilk.*, Nov., 1872) regards the cheesy products as specific, miliary tubercle as a secondary product of cheesy transformation. The first, according to him, is the specific tuberculous inflammation. This forms more or less circumscribed infiltrations of the connective tissue. The infiltration consists of cells, which are distinguished from pus-corpuscles by their abundant, finely-granular protoplasm, and which do not, like pus-corpuscles, come from the bloodvessels, but from the fixed cells of the connective substance and endothelium, perhaps also from smooth muscular fibres, and the epithelium of the lungs and kidneys. The nucleus of these cells, with the immediately adjacent protoplasm, secretes something peculiar, and swells into a tubercle-cell, while the remainder of the cell disappears. Upon this PRIMARY affection, with the character of phthisis or ulceration, there follow the SECONDARY affection, which consists in an infection of the neighborhood and corresponding lymph-glands, and the TERTIARY affection, which is the expression of an infection of the whole organism (miliary tubercles of most different organs).

Besides cheesy inflammation, blood-effusions also, with retention of the blood and consecutive drying and cheesy transformation, have been looked upon as causes of secondary tuberculosis. Neither experiment (see p. 221) nor pathologico-anatomical and clinical investigations have furnished certain proofs of this.

After INOCULATION, miliary tubercles have been found in various organs, and indeed after inoculation of true tubercular substance as well as of tuberculized inflammations, of diseased and healthy tissues of all kinds, of substances not animal (*e.g.*, paper). About the substance introduced into the abdominal or thoracic cavity or under the skin, there appears an unencapsuled focus, filled with mucous pus. The taking-up of this by the lymphatics and bloodvessels appears to be the condition of the secondary tubercle-formation. The latter is present in from twenty to fifty days after inoculation. Miliary tubercles are found in at least three organs, which differ with the mode of inoculation : most often in the lymph-glands nearest the point of inoculation and the corresponding serous membrane, in the lungs and liver, somewhat more rarely in the spleen, kidneys, intestines, etc. The tubercles are macroscopically similar to miliary tubercles. Most affirm the microscopical identity of tubercle from inoculation, while others deny or doubt this, either with respect to all or many of them. Inoculation appears to succeed better, if small quantities of a not too irritant character are employed, while larger quantities and substances more strongly irritant com-

monly give rise to stronger inflammation and suppuration, but not to tuberculosis.

Besides by inoculation, tuberculosis has been produced by the use of tuberculous masses as FOOD. Finally, it is probable that the MILK of tuberculous animals generates tuberculosis in those nourished by it. Likewise the pearly sickness of cattle, a disease in general similar to tuberculosis, causes true tuberculosis.

The INOCULATION OF TUBERCULOSIS has during late years been a daily question. Disregarding the earliest experiments with inoculation by KORTUM (1789). CRUVEILHIER (1826), and others, also disregarding the experiments connected with the inoculation of glanders and farcy and their artificial production by LEVELL VINES, RENAULT-BONNEY, and others, we have the discovery in 1834 by ERDT (*Die Rotzdyscr.*, 1863) of numerous knots in the lungs of horses after inoculation with scrofulous pus of man, by KLENCKE (1843) of pulmonary and hepatic tuberculosis in rabbits, through injection of tubercle into the cervical veins, also by LEBERT (1851) of similar results in dogs after injection of pus into the veins. But the greatest interest was excited by the communications of VILLEMIN (1865). V. introduced partly gray, but for the greatest part yellow tubercle-masses and cheesy pneumonic substance, also those substances from man or animals, finely triturated, once or many times, under the skin of different animals, and, from ten to twenty days thereafter, found fresh tubercle in the lungs, still later also in the intestines, mesentery, etc., especially in rabbits and guinea-pigs. From this he concludes that tuberculosis is a specific, virulent disease. A. VOGEL with horses, and especially LANGHANS (*die Uebertragb. d. Tuberc. auf Kaninchen*, 1868) with rabbits, BIFFI, VERGA, SANGALLI with mules, cows, sheep, dogs, mice, could not obtain the same results. On the other hand, HÉRARD and CORNIL (*Union méd.*, 1866, Nos. 128 et 130), HOFFMANN (l. c.), COLIN, BÉHIER, EMPIS, MANTEGAZZA, BIZZOZERO, LEBERT, and WYSS (*Virch. Arch.*, XL., p. 200; XLI., p. 540), KLEBS, KÖSTER, WALDENBURG, BIJNEN (*Nederl. Tijdschr.*, 1868, p. 255), SIMON and SANDERSON, W. FOX, PAPILLON, NICOL and LAVERAN, and others, succeeded in many inoculations with the same or similar substances (cheesy pneumonic lungs, cheesy hypertrophic lymph-glands, cavernous and bronchial secretions, etc.), with substances of different kinds not tuberculous, also those which had lain in alcohol. SIMON and SANDERSON saw miliary tubercle also in consequence of suppuration after the use of setons, which had been applied for a long time.

COHNHEIM and FRÄNKEL found miliary tubercles in the peritoneum (the place of inoculation), liver, spleen, pleura, lungs, etc., not only after inoculation of tuberculous substances, but also after that of any portion of dead bodies or of any kind of substance (blotting-paper, gutta-percha, etc.). In favorable cases there appeared in the inoculated animals, mostly guinea-pigs, about the inoculated body a focus limited by a vascular capsule, and filled with an odorless, white, tenacious substance. According to the authors, it is the dead and inspissated pus, the taking up of which into the circulation causes the formation of tubercle. (This metamorphosis of pus is frequent in rabbits, guinea-pigs, etc., rare in dogs, on account of which in the latter tuberculosis arises only when inspissated pus is injected directly into the humors.) The tubercle had therewith lost its specific character. The old strife, whether tubercle is a specific new-formation (BAYLE, VIRCHOW, BUHL, VILLEMIN, KLEBS, and others) or a product of inflammation (BROUSSAIS, REINHARDT, COHNHEIM, NIEMEYER, and others), seems thereby at least in part to be set at rest.

And yet KLEBS, BERNHARDT (*D. Arch. f. klin. Med.*, 1869, V., p. 568), and others reached somewhat different results. The latter found that disinfection of the tuberculous substance, inoculated from man as well as from rabbits, diminished its infectiousness to a high degree. Tuberculosis may accordingly be traced back to mechanical causes (capillary embolisms of metamorphosed products of inflammation—WYSS), or it arises through taking up very finely divided particles, smaller or at least not larger than blood-corpuscles, into the blood and their deposition into various organs (WALDENBURG). Probably these particles act only or chiefly in a mechanical manner. This view is supported also by the predilection of the inoculated tubercle to lie in proximity to the vessels and even the vessel-wall (FOX, WYSS, WALDENBURG).

Some other experimental pathological facts, like the assumptions of PANUM (*Virch. Arch.*, XXV., p. 487) and DENKOWSKI (*Med. Ctrlbl.*, 1865, No. 3), are still more doubtful.

Further, the generation of tubercle has been experimented on, not only by inoculation, but by feeding, with similar results : CHAUVEAU, AUFRECHT (*Med. Centralbl.*, 1869, No. 28), and others.

Through experiments on inoculation of tuberculosis, an importance has been given anew to a disease of cattle, which bears manifold resemblance to tuberculosis of man: this, the so-called pearly sickness or French disease of cattle is, according to VIRCHOW, a lympho-sarcomatosis; according to LEISERING (*Ber. üb. d. Veterinärwesen in Sachsen*, 1864), GERLACH, FUCHS, ZÜRN, and others, it is a true tuberculosis. According to SCHÜPPEL (*Virch. Arch.*, 1872, LVI., p. 38), it is histologically identical with tuberculosis. It is distinguished by this, that the reticulum does not undergo retrograde metamorphosis, and that the pearly knots become calcified throughout and very early. It always appears primarily on the diaphragm and peritoneum, then attacks the lymph-glands, especially of the breast and abdomen, rarely, and for the most part in slight degree, the parenchyma of the lungs, liver, and Fallopian tubes. CHAUVEAU first showed that the pearly sickness of cattle is transmissible to cattle. KLEBS (*Virch. Arch.*, LI., p. 291) found that guinea-pigs, after inoculation of matter generated by the pearly sickness, were affected by general tuberculosis, and that calves, inoculated with human tubercles, were affected by pearly knots. GERLACH, HARMS and GÜNTHER, and LEISERING obtained analogous results. GERLACH (*Virch. Arch.*, 1871, LI., p. 290) fed two calves, two swine, one sheep, and two rabbits with the milk of a cow affected by pearly disease. With the exception of one animal, there were found in the four different kinds of animals, swellings and tuberculous degeneration (gray nodules, small cheesy foci, and deposits of lime salts) of the mesenteric glands, and miliary tubercles in the lungs. LEISERING (*Ber. üb. d. Veter.*, 1870) found that also boiled matter of pearly sickness was inoculated with success. From the experiments above given and from his own, ZÜRN (*Zoopath. u. zoophysiol. Unters.*, 1872, p. 1) draws the following conclusions: subcutaneous or peritoneal inoculation of the matter of pearly disease generates miliary tuberculosis in swine, rabbits, and sheep;—feeding with this matter has the same effect;—the pearly disease of cattle owes its origin to the same virus as tuberculosis of man ;—feeding with this matter boiled acts like that not boiled ;—the raw meat of animals strongly diseased with the pearly disease may infect healthy animals, boiled meat probably not.

According to KLEBS (*Arch. f. exp. Path.*, 1873, I., p. 163), it is only an admixture of cheesy pus which produces tuberculosis. The milk of tuberculous cows generates tuberculosis in different animals. It usually begins with intestinal catarrh, then leads to tuberculous affections of mesenteric glands (scrofulosis), also to tuberculosis of the liver and spleen, and finally to extended miliary tuberculosis of the thoracic organs. Thus is the course the same as that of human scrofulosis and secondary tuberculosis. Tuberculous infection by milk may be overcome by a strong organism, as the already formed tubercle may be resorbed or healed by the formation of cicatrix. The tuberculous virus is present in the milk of sick cows. It is found in form of solution in the serum of the milk. It is probably not destroyed by the common, not very careful mode of cooking.

RUGE (*Beitr. z. Lehre v. d. Tuberc.*, Berl. Diss., 1869) found that idiopathic tuberculosis occurs in guinea-pigs. He also demonstrated (against SANDERSON, FOX, COHNHEIM, and others), that tuberculosis may appear after inoculations, without the presence of pus-focus dependent upon the operation and introduction of a foreign body.

From the experiments of BOGOSLOVSKY (*Med. Ctrlbl.*, 1871, No. 7), who inoculated various animals with the serum only or only the formed elements of the same tuberculous pus, it was shown that only the latter were effectual.

Accurate histological investigation of tubercle of inoculation was neglected by most, and the statements of KÖSTER (*Verh. d. Würzb. phys.-med. Ges.*, June, 1869) appear to justify many experimenters. Others describe tubercle from inoculation accurately, and regarded it as composed in the old manner. According to FOX and SANDERSON, tubercle is equivalent with cytogenic or adenoid tissue. According to S. the tubercle from inoculation of the pleura, peritoneum, etc., is not an absolute new-formation, but a hyperplasia of normal, very small lymph-nodules. KLEBS and AUFRECHT found giant-cells in it.

The inflammatory affections often occurring in man with miliary tubercle, were also often found in tuberculosis from inoculation, as it appears, especially if the inoculated matters were adulterated with mechanical or chemical irritants.

SCROFULOSIS.

SCROFULOSIS is a disease especially of CHILDHOOD and youth. It is either congenital and occurs in the children of scrofulous or aged or nearly related

parents, or in tertiary syphilis, tuberculosis, etc., of the parents, especially of the mother. Or it is ACQUIRED: by cold, moist, badly ventilated, sunless abodes, unsuitable nourishment, little movement of the body, by preceding severe sickness in the first months of life (measles, whooping-cough). It rarely appears before the end of the first, mostly in the second and third years of life, not infrequently still later.

The SYMPTOMS of scrofulosis are: inflammations of the skin, in the sub-cutaneous cellular tissue, of the bordering mucous membranes: eruptions on the skin, especially of the head and face, chiefly in the region of the nose, mouth, eyes, and ears, mostly of an eczematous or impetiginous form; in-flammations of various kinds of the eyes, often with great photophobia; discharges from the ears; catarrhs of the mouth and throat; inflammations of the bones, including the joints, sometimes only of the periosteum, some-times of the bone itself, not infrequently with termination in caries or necrosis, most often of the vertebræ, of the small bones and joints of the extremities; inflammations in the external, more rarely in the internal (previously normal or hypertrophic) lymph-glands, sometimes of the com-mon character of cellular hyperplasia, sometimes with simultaneous forma-tion of pus, sometimes with formation of miliary tubercles. The cheesy masses of the lymph-glands are of the most varying size: sometimes hardly visible, sometimes of the size of a pea and larger, sometimes involving the whole gland. All these inflammations run their course SLOWLY, and lead with a for the most part slight hyperæmia to common DRY SUPPURATION and ULCERATION; those of the lymph-glands easily pass to the limiting mem-brane, or mucous membrane. For the most part the face presents a bloated appearance, the lips and nose are thick, as if œdematous, the skin dirty-pale, the subcutaneous cellular tissue comparatively rich in fat, the muscles spare, the abdomen prominent, the extremities thin: so-called TORPID scrofulosis. More rarely is there emaciation and a moderate red-dening of the skin: so-called ERETHISTIC scrofulosis. In both cases the quantity of the blood in general is diminished. Especial blood-changes are not known.

The individual affections of the scrofulous perhaps have, according to the older view, nothing peculiar. This holds good of inflammations, as well as of non-inflammatory swellings. The latter are sometimes more like chronic œdematous infiltrations, sometimes more like œdematous connective-tissue hypertrophies. Characteristic of it, however, are: the great ease of its ap-pearance (so-called vulnerability of tissues), the obstinacy of its duration (mostly for years), or of its return without demonstrable cause, the ease with which the lymph-glands participate (at the beginning in form of an enlargement of their cells and of an increase of them, later in form of cheesy transformation and secondary softening), and the length of time with which suppuration of the latter outlasts the primary affections of the skin and mucous membranes.

The termination of scrofulosis is, in its lower grades, for the most part, recovery, in its higher grades not infrequently death. The latter results: through scrofulous, or tuberculous suppurations, or through miliary tuberculosis of internal organs (mesenteric and bronchial glands for the most part with, rarely without tuberculosis of the intestines and lungs); through severe suppurations of the joints and bones with consecutive maras-mus or with lardaceous degeneration of different organs; rarely through general anæmia.

Scrofulosis and tuberculosis are held by many to be identical, by others to be different. More recent investigations have shown that there is no

essential histological distinction between tuberculosis and scrofulosis of the lymph-glands. This identity is supported by: the frequently simultaneous occurrence of tuberculosis and scrofulosis ; the circumstance, that scrofulous children not infrequently become tuberculous; that scrofulous new-formations resemble the tuberculous, not only of themselves, but also in their most frequent metamorphoses (cheesy transformation or simple atrophy).

According to KLEBS, forms of disease of the lymph-glands may be produced by inoculation of tuberculous matter, which forms of disease bear a perfect resemblance to scrofulous forms of disease of the glands in man.

Consult, on the histological relations, SCHÜPPEL (*Unters. über Lymphdrüsen-Tuberc.*, 1871). According to SCH., cheesy metamorphosis of the lymph-glands depends upon the presence of tubercles. The latter are found always and exclusively in the vascular follicles of the glands, and have the structure above given. Their further fate is most frequently necrosis of the cells as well as of the reticulum, more often with subsequent softening, less frequently with encapsuling or with deposit of calcareous salts ; resorption rarely occurs, and only to a limited extent.

2. LYMPHATIC NEW-FORMATION, LYMPHOMA.

VIRCHOW, *Fror. Not.*, 1845, p. 780 ; *Arch.*, 1847, I., p. 569; V., pp. 58 et 125 ; *Würzb. Verh.*, I., p. 81 ; VII., p. 115 ; *Die krkh. Geschw.*, II., p. 559.—BENNETT, *Edinb. Med. J.*, Oct., 1845.—BUHL, *Ztschr. f. rat. Med.*, 1856, VIII.—E. WAGNER, *Arch. f. phys. Heilk*, 1856, p. 441 ; *Arch. d. Heilk*, I., p. 322; II., p. 103 ; V., pp. 90 et 262.—FRIEDREICH, *Virch. Arch.*, 1857, XII., p. 37.—BÖTTCHER, *Virch. Arch.*, 1858, XIV., p. 483 ; XXXVII., p. 163.—VOLKMANN, *Abh. d. Naturf. Ges. in Halle*, 1858.—BECKMANN, *Virch. Arch.*, 1860, XIX., p. 537.—DEITERS, *Deutsche Klinik*, 1861, Nos. 15, 18, 19, 22.—FÖRSTER, *Würzb. med. Ztschr.*, III., p. 203 ; *Lehrb. d. path. Anat.*, 6. Aufl., 1864, p. 119.—RECKLINGHAUSEN, *Virch. Arch.*, 1864, XXX., p. 370.—SIMON, *Med. Ctrlbl.*, 1868, No. 53.—HOFFMANN, *Unters üb. d. path.-anat. Ver. d. Orgg. beim Abdom.-Typh.*, 1869.—NEUMANN, *Arch. d. Heilk.*, 1870, XI., p. 1 ; SCHMIDT's *Jahrb.*, XCVII., p. 203; CXII., p. 33 ; CXV., p. 175.—WALDEYER, *Virch. Arch.*, 1871, LII., p. 305.—WOLFFHÜGEL, *Zur Kenntn. leukäm. Neubild.*, *Würzb, Diss.*, 1871.—PONFICK, *Virch. Arch.*, 1872, LVI., p. 534.

(See besides, the literature of typhoid fever and leucocythæmia.)

LYMPHATIC NEW-FORMATIONS are nearly always small, even microscopical, rarely larger, appearing in form of tumors, or as infiltration, white or gray-white, for the most part soft, rarely firm. They consist of small or medium-sized, rounded, bright nuclei, and, as a rule simultaneously, of small cells, which are similar to lymph-corpuscles or colorless blood-corpuscles; sometimes, however, they are larger. Both lie, in varying quantity and with an abundant or scanty, for the most part semi-fluid, rarely at points or wholly fibrous intermediate substance, between the normal elements.

Lymphatic new-formation shows manifold, in special cases sometimes not recognizable transitions to granulation-tissue, on the one hand, but is to be distinguished from it by this, that it is never transformed into connective tissue (see p. 380); nor, on the other hand, to hyperplastic or even to heteroplastic new-formation of cytogenic tissue (see p. 440).

Lymphatic new-formations occur constantly in typhoid fever, frequently in leucocythæmia, sometimes also in measles, scarlatina, and variola, in puerperal fever, diphtheria, chronic diseases of the heart, Bright's disease, etc. They are often found in the granulation-tissue of every locality, as well as in many connective-tissue hypertrophies of the skin.

In TYPHOID FEVER these new-formations form the only essential anatomical condition in the small intestine, in the corresponding mesenteric glands, in the spleen, not infrequently also in the liver, sometimes in the large in-

testine, in the kidneys, the peritoneum, the laryngeal mucous membrane,
etc. In the intestinal canal and mesenteric glands there arise thereby the
known pulpy infiltration, in the spleen the soft swelling, in the liver, kid-
neys, and peritoneum various numerous, for the most part small, even
microscopical, gray or white, soft granules.

The new-formed nuclei and cells have sometimes the significance of an increase of
gland-juice, as in the solitary follicles of the large and small intestines, in Peyer's
patches, in the lymph-glands of the mesentery, liver, spleen, kidneys, bronchi, spleen ;
sometimes they form an infiltration, or have the form of very small, gray-white, soft,
isolated or confluent granules. This is the case in the capsule of the intestinal fol-
licles, in the connective tissue of the mucous, sub-mucous, muscular, subserous, and
serous tunics around the affected follicles of the intestine, in the capsule of the
lymph-glands, in the connective tissue surrounding these, in the connective tissue of
the hilus of the glands, in the liver, where the granules are met with in the interior
of the acini or in the sheaths of the vessels, in the kidneys, where they occur espe-
cially in the cortical substance, in rare cases also in the mucous membrane of the
urinary passages, and in the peritoneum at a distance from the affected follicles.

With respect to the DESTINY and the METAMORPHOSES of lymphatic new-
formation, we know them only as they occur in typhoid fever. In what
relation it stands to the constantly accompanying general affection is not
known.

Lymphatic new-formation in typhoid fever is either resorbed by way of fatty
metamorphosis : the most frequent process. Or, there appears a simple atrophy of
it, sometimes with fatty metamorphosis : sloughing, especially on the intestinal mu-
cous membrane. Or, softening appears through increase of the fluid basis substance.
Or, there appears calcification.
HESCHL (*Wien. med. Wschr.*, 1871, No. 34) found in the typhous infiltration of the
intestines, in the mucous membrane within the very distinct, often isolated *adventi-
tia capillaris*, the nuclei in the vessel-wall swollen to three times their diameter and
twice their length, projecting from all sides into the lumen of the vessels, the latter
correspondingly narrowed, and wavy; the dilated vessels were densely filled with
blood-corpuscles. Many capillaries were wider, provided with enlarged nuclei, and
contained white and red blood-corpuscles : the former in comparatively larger num-
ber ; many of these were far larger (two to three times) than normal, and resembled
the larger cells of typhoid infiltration found outside of the vessels. All this explains
the SLOUGH-FORMATION, since the narrow portions of the capillaries cannot be passed
by the enlarged blood-corpuscles. (H. saw a similar thing long ago in inflammatory
induration of the lungs.). In the longitudinal muscular layer, H. found quite con-
stantly an increase of the muscular nuclei. The muscle-cells commonly divide into
many parts, which finally assume the form of other typhous cells, and between the
muscular bundles form nests of cells.

In OTHER CONTAGIOUS DISEASES, only in some cases has lymphatic new-
formation been found, especially in those of the liver and spleen, rarely of
other organs. In variola vera it is most constant in the spleen in form of
round nodules or branched striæ which correspond to the distribution of
the vessels.

ROTH (*Virch. Arch.*, 1872, LIV., p. 254) found, in a very chronic case of pharyn-
geal diphtheritis, in part large lymphatic growths in the kidneys, liver, submucous
coat of the stomach and intestines, larynx, cellular hyperplasiæ in the spleen and
lymph-glands.

LEUCOCYTHÆMIC NEW-FORMATIONS occur most frequently in the spleen
(so-called LIENAL leucocythæmia), in the lymph-glands (so-called LYMPHA-
TIC leucocythæmia), and probably in the medulla of bones (so-called MYELO-
GENIC or MEDULLARY leucocythæmia), more rarely in the liver, rarely in

the kidneys, mucous membrane of the stomach, jejunum, ileum, rectum, the great air-passages, in the pleuræ, peritoneum, pericardium, periosteum, tonsils, choroid, brain (so-called NEO-PLASTIC leucocythæmia). The spleen and lymph-glands thereby become uniformly, and not infrequently to five and even twenty times enlarged. The leucocythæmic spleen occurs in two forms : in the diffuse form the cellular growths are uniformly distributed through the spleen in the arterial sheath ; while in the other form the lymphoma-formation affects only the follicles of the spleen. The bone-marrow (of tubular bones as well as of the sternum, ribs, and vertebræ) is uniformly greenish-yellow, but in the air is grayish-red. In the remaining organs there are found for the most part small, sometimes microscopical, round, spherical (sometimes like miliary tubercle), more rarely larger, flat round, branched or directly infiltrated masses. They for the most part show no essential change, or only slight simple atrophy or fatty metamorphosis ; leucocythæmic ulcers and cavities rarely occur. They are for the most part chronic, in very rare cases acute.

The more immediate relation of leucocythæmic new-formations to increase of colorless blood-corpuscles is not yet known.

DEITERS communicates a case anomalous in many respects, and important on account of its relation to leucocythæmia. He found lines of spindle-shaped cells, of which the most external layers were used in the formation of the capillary wall, the internal in the formation of lymph-cells.

OLLIVIER and RANVIER (*Gaz. méd. de Par.*, 1867, No. 24) regarded lymphatic new-formations in various organs in leucocythæmia as arising through bursting of the bloodvessels, exit of lymphoid corpuscles and increase of them at the place of their escape. EBERTH (*Virch. Arch.*, XLIII., p. 8) questions whether the elements of leucocythæmic growths may not be direct descendants from the blood. KÖSTER (*Med. Centr.*, 1868, No. 2) holds that in leucocythæmia the colorless blood-corpuscles penetrate into serous membranes and cavities. But he could not convince himself with respect to a new-formation in serous connective tissue. Also the lymphoid cells occurring in leucocythæmia in interstices of organs (liver, kidneys) he regards as emigrated colorless blood-cells.

KLOB (*Wien. med. Wochenschr.*, 1862, No. 35 et 36) objects to the assumption of the so-called leucocythæmic tumors of the lymph-glands : 1, that a blood-change analogous to that in lymphatic leucocythæmia occurs also without lymph-gland tumors ; 2, there are sufficiently precise observations of very considerable hyperplasiæ of lymphglands without a corresponding blood-change. According to K. there are no specific tumors belonging to leucocythæmia or dependent upon it, consequently also no leucocythæmic tumors.

BRIIL (*Lungenentz*, etc., 1872, p. 133) first drew attention to the frequency of LYMPHOMA-FORMATIONS IN EMBRYONIC CONNECTIVE TISSUE (granulation connective tissue) ; that lymphomata occur in corresponding inflammations of serous membranes, etc., so much the more certainly as the new-formation, in opposition to the intercellular substance, is richer in cells. Generally there is a more extensive embryonic connective tissue new-formation without lymphoma-formation. If the lymphomata are few in number, they become resorbed.

XII. NEW-FORMATION OF (TRUE) EPITHELIUM.

The literature is found in that of healing of wounds (p. 377), as well as in that of some new-formations consisting of epithelium, especially adenoma and epithelial cancer. The epithelium of the organs of sense, as the rods, etc., of the retina, are left out of consideration in the following remarks.

NEW-FORMATION OF TRUE EPITHELIUM is of frequent occurrence. It embraces all those formations which in the normal development of the body proceed from the external germinal layer (exclusively of the nervous system) and from the internal germinal layer : thus the epidermis with the

rete Malpighi, the cutaneous glands, the hair, the epithelium and glands of
the mouth, throat and nose, the crystalline lens, the kidneys, and genital
glands; also the gastric and intestinal epithelium, intestinal glands, liver
and epithelial elements of the respiratory system.

(On the new-formation of so-called false epithelium, see p. 394.)
Under normal conditions, the distinction between true and false epithelium (so-
called endothelium) is easy at least in those parts which are of interest to us.   Under
pathological conditions, on the other hand, this is not infrequently difficult or even
altogether impossible.   The following characteristics belong to true epithelium :
origin from the external or internal germinal layer ; true epithelial cells are always
connected, but only by an intercellular substance, a cement ; they contain no blood-
or lymphatic vessels (WALDEYER).
His distinguishes only two germinal layers, the archiblast and the parablast.   The
former has its origin from the cells of the ovum, the latter from the white yolk.
The archiblast embraces all tissues, except vessels (with blood) and connective sub-
stances.

Concerning the form and locality of pathological new-formation of true
epithelium, and of forms derived from it, there are three opposite views :
the one, which makes this epithelium, etc., to arise only from pre-existing
epithelium of the external or internal germinal layer, which thus transfers
the normal processes of development to pathological processes ; the other,
which besides this genesis assumes another origin of true epithelium from
connective tissue, and either by growth, etc., of the connective-tissue cor-
puscles, or by metamorphosis of migratory cells into epithelial cells, thus
from elements of the middle germinal layer; and the third, whereby the
epithelium arises from free blastema, which is a product of the epithelium
or of the subjacent tissue.   The first view is by far the best supported
theoretically, as well as by experimental investigations, observations on the
dead body and in the sick.   (See p. 361.)

New-formation of epithelium occurs likewise in form of regeneration,
hypertrophy, and tumor.   Both of the latter forms, however, have such
manifold transitions, that a separate consideration of them is for the most
part impossible.

New-formed epithelia are found either in localities where it occurs
normally, as in the skin and mucous membranes, in true glands ; or they
grow into other forms of tissue, e.g., epithelium of mucous membrane
into mucous and submucous tunics, etc. (so-called heterotopia).   They
repeat in both cases either the normal gross and fine forms (homologous
new-formations) ; or they depart from it more or less (heterologous new-
formations, glandular tumors, many cysts, epithelial cancers).   They occur
finally either alone, or there is developed with them simultaneously vas-
cular connective tissue.

1. NEW-FORMATION OF EPITHELIUM ALONE.

A. NEW-FORMATION OF EPITHELIUM AS REGENERATION.

A regeneration of epithelium of every kind is of very frequent occurrence.
If the epithelium is poly-laminar, as on membranes, etc., and the upper
epithelial layers only are destroyed, while the lowermost remain, as is the
case in traumatic erosions of the skin and mucous membranes, in many
catarrhal inflammations, regeneration probably takes place in the same
manner as under normal conditions.

But in those cases, where all the layers of the epithelium are destroyed,

the conditions of regeneration are complicated. That such a regeneration does take place, is shown by thousands of observations on the skin and external mucous membranes, as well as by many experimental investigations. In healing wounds of every kind of the skin and mucous membranes, epithelial regeneration usually takes place from the borders of the wound : so-called BORDER or PERIPHERAL restoration of the skin ; more rarely alone or at the same time separated from the borders of the wound in one or more points : so-called INSULAR or CENTRAL restoration. The former takes place only in a comparatively limited manner : it appears usually on this account much more important, because, simultaneously with the restoration of membrane, there follows the so-called cicatricial contraction of the whole surface of the wound. With respect to the latter, insular masses of epidermis, especially in gangrenous wounds, are observed upon the granular surface : these correspond most probably to points where the papillæ with the immediately adjacent epithelium are in part preserved.

The histological conditions of epithelial regeneration have only recently reached a certain conclusion. Regeneration takes place most probably only from those epithelial cells which lie near, i.e. under the loss of substance. According to one view, the bordering epithelia are twofold and more enlarged, divide after previous increase of nuclei, and grow into the space left by the loss of substance. According to the other view, the epithelia remaining behind push out nuclear processes, which are thickly developed near the mother-cells, or penetrate between the neighboring epithelial cells, thereby also pushing forward old epithelial cells, and finally become independent. The remaining theories of epithelial regeneration are without well-founded microscopical proofs.

ARNOLD (Virch. Arch., 1869, XLVI., p. 168) has investigated the regeneration of epithelium in the tongue, cornea, and foot-web of the frog, as well as on the palate and scalp of the dog, with and without previous injection of cinnabar into the blood. He found on the hard palate in the restoration of the membrane over parts where there were deep losses of substance, a formation of isolated islands of epithelium. According to A., the epithelial spaces were entirely or only peripherically filled with a finely granular substance, which at the border of the epithelium is metamorphosed into a glassy, peculiarly refractive mass. This consists for the most part of single or many flat, more rarely of more globular epithelial cells, which lie with one surface on the subjacent tissue, while the other surface is free or covered by other epithelial cells. In these masses phenomena of division now appear, like those in the ovum : light lines pass through them and divide them at first into larger, very soon into smaller rounded or angular sections, which have the size of one or of from three to six epithelial cells. In the plates thus defined there immediately appear bright bodies (nuclear corpuscles) ; these are bounded by ill-defined circles, the first phenomena of a nucleus formation, finally a complete nucleus. During these changes, very fine granules are seen in the light substance of the surface. Thus finally the epithelial cell becomes complete. The finely granular substance, out of which the protoplasm is formed by metamorphosis, is either a product of secretion of the epithelial forms lying at the border ; or it is a product of the corneal tissue, skin, and mucous membrane. A. regards the latter as the more probable.

WADSWORTH-EBERTH, HOFFMANN, and others have opposed this view.

Most surgeons hold fast to a DOUBLE ORIGIN of EPITHELIUM : partly from the normal epithelium of the borders of wounds, partly from the uppermost granulation-cells. They support the latter view, especially on the occurrence of epithelial islands separate from the borders of the wound, in part also on the still doubtful microscopical facts. Others, on the other hand, especially THIERSCH (Der Epithelialkrebs, 1865 ; —Pitha-Billroth's Hdb. d. Chir., I., 2. Abth., p. 531), according to him, also WALDEYER (Virch. Arch., XLI., p. 470), hold the source of new epithelium to be only pre-existing epithelia : either from the epithelia still remaining in or under the granulating wound-surface (e.g., in superficial wounds in the portion of the stratum Malpighi depressed between the papillæ, or by growth inward from the epithelia of the

borders of the wound. TH. supports his view on this, that in wounds of the skin the bordering restoration of membrane is only one to two cent. broad, that then the capacity of the pre-existing epithelium to further production is exhausted, which the view of his opponents makes improbable. TH. likewise saw in rare cases epithelial islands on well-protected granulations, where every co-operation of pre-existing epithelium was impossible; but these restorations of the surface again disappeared after a few hours' or a single day's existence.

The view defended by many, that the ORIGIN OF EPITHELIAL CELLS IS FROM FIXED CORPUSCLES OF THE SUBJACENT CONNECTIVE TISSUE, by direct metamorphosis, or after preceding increase, is neither histologically nor experimento-pathologically founded. F. A. HOFFMANN (Virch. Arch., LI., p. 373) introduced cinnabar through the sclera into the anterior chamber of the eye of a frog, and found after seven to fourteen days the same in the anterior epithelium. But perhaps the granules were transported hither by the transudation and increased intra-ocular pressure. If cinnabar is introduced into the blood, it is found after twenty-one to twenty-five days in the fixed corneal corpuscles, but not in the corneal epithelium, not even after thirty to fifty days.

The ORIGIN OF EPITHELIUM FROM MIGRATORY CELLS has likewise found supporters, but is demonstrated neither histologically nor by injection of coloring matters into the blood. It is supported by the regular occurrence of such cells between the normal epithelia, as well as by their increased number in epithelial membranes, in which regenerative processes take place alone or simultaneously, also with inflammatory processes (ARNOLD and others). They lie here between the epithelia, and are easily recognized as long as they are not dead, and thereby have become granular and globular, by their brightness, their irregular form, and their processes. On the significance which belongs to migratory cells in regeneration, vide infra.

With respect to the origin of epithelium from epithelium remaining intact, many experimento-pathological investigations as well as surgical experience support it. In both cases the injury is followed besides by the regenerative, almost always also by inflammatory processes: thereby there arise two forms of also histologically different products, which are with difficulty or not at all to be kept distinct.

According to CLELAND (Journ. of Anat. and Phys., 1868, II., p 361), the corneal epithelium is regenerated from the same and also from its middle layer.

HELLER (Unters. üb. d. fein. Vorg. bei d. Entz., Erl., 1869, p. 28) has directly observed the division of epithelial cells (at first of the nucleoli, then of the nuclei) and their migratory character during restoration of the epithelium of wounds of the tongue.

WADSWORTH and EBERTH (Virch. Arch., 1870, LI., p. 361) separated the corneal epithelium in the frog by tincture of cantharides, collodion or ether, also in rabbits and guinea-pigs, at the same time with removal of the most external lamella of the cornea. A few days after, regeneration of the epithelium appeared in the following manner. The epithelia bordering the loss of substance, probably also some epithelia remaining in the continuity, BECAME TWO TO THREE FOLD LARGER and DIVIDED, after a previous increase of the nuclei (by division or free nucleus-formation), without the assistance of free protoplasm, and GREW into the space occasioned by the loss of substance. Even small islands of corneal epithelium, if they are quite removed from the vascular organ, continue to live, and produce new epithelium though more slowly than epithelium remaining after central losses.

F. A. HOFFMANN (l. c.) experimented likewise on the cornea of the frog and rabbit. According to him, new epithelium arises by a proliferation of the epithelia still present. These PUSH FORWARD PROCESSES and are closely developed by side of the mother-cells, or penetrate between neighboring epithelial cells on the side of the least resistance. Probably there exist the most manifold transitions between division in the common sense and constriction after budding. H. never saw processes connected with the cells of the lowest layer; they arise perhaps from those lying above. According to this view, the space is not entirely closed by new cells, but by the young cell-processes, which are formed to a great extent, penetrate also old cells, so that in a certain stage there is found a wonderful mosaic of old and young cells extended over the whole cornea. Preparative to this is the action of the migratory cells; they, in the first stage of the reaction, reach into the epithelium, loosen it, lead to the formation of very small open spaces; these later become filled by epithelial cell-processes, i.e. young epithelia.

HEIBERG (Oestr. Jb., 1871, 1. H., p. 7) investigated the new-formation of corneal epithelium, which had been scraped off, especially in the frog, also in hens and rats. Restoration follows in frogs before the end of the third, in birds, etc., before the end

of the first day. Regeneration of the defect proceeds always from the borders. The migratory cells have no share in this. The epithelia immediately adjacent to the epithelial defect push forward irregular, unequally long, and short, knobbed processes, which project into the spaces. The knobs change their form, but much more slowly than in amœboid movements. In the processes there appear small, strongly refractive, round globules, like nucleoli. Many processes collect into homogeneous, clear globules or round plates and separate. The processes arise from the surface, as well as from the deeper lying epithelial layers.

KRAUSE (*Arch. f. Anat., Phys. u. wiss. Med.*, 1870, p. 232) found in investigations of successive cut surfaces in the anterior epithelium of the cornea. that the cell-new-formation did not take place in the lower cell layers, but first began in the third layer. In the epidermis of mammals it is the so-called middle layer, *i.e.*, the parts of it lying closely beneath the corneal layer, to which the reproduction of the external horny layers is under normal conditions ascribed.

In the skin, the conditions of epithelial regeneration are, according to SCHRÖN (*Contrib. alla anat., fisiol. e pathol. della cute umana*, 1865), still more complicated. SCH. assumes, with OEHL, three layers of cutaneous epithelium : the stratum Malpighi, the stratum pellucidum (proceeding from the uppermost layers of the Malpighian layer), and the stratum corneum (epidermis proper). The latter is regarded by SCH. as a product of the sweat-, perhaps also of the sebaceous glands. According to SCH., the restoration of the surface of cicatrices always consists only of the stratum Malpighi and stratum lucidum, if no sweat glands are present in the extent of the wound; on this account the cicatrix remains smooth and shining. And yet irregular lamellar epidermis-like masses may be formed thereon (hypertrophic stratum lucidum—RINDFLEISCH calls them cicatricial epitheliomata). In superficial injuries of the skin, the sweat-gland coils remain for the most part uninjured ; since these glands produce only corneal cells, a complete regeneration of the epidermis is possible. AUFFHAMMER (*Verh. d. Würzb. ph.-med. Ges.*, 1869) has refuted for the most part SCHRÖN's statements.

According to LOTT (*Med. Ctrlbl.*, 1871, No. 37), in regeneration of the corneal epithelium from the so-called pedal plates of the so-called pedal cells [*Fusszellen*] (ROLLETT), by gradual growth of nucleated portions of protoplasm, are separated and are shoved farther upward.

Consult also SCHÜLLER, *Virch. Arch.*, 1872, LV., p. 159.

In closest relation with epithelial regeneration from epithelium, stands the practice during late years of TRANSPLANTATION (without bridge-forming : see p. 381) of small portions of skin and mucous membrane on granulation-surfaces. This, since its discovery, has been many times performed with the best results in large cutaneous ulcers, which heal with difficulty or not at all, in large accidental or intentional losses of cutaneous substance, to lessen cicatricial contraction, etc. The pieces of skin transplanted on wounds consist of cutis together with epithelium. The former unites with the subjacent portions of skin by first intention, the horny layer of the epithelium is thrown off, new epithelium is formed from the rete Malpighi on the bordering surface of the wound, for the most part in the form of needles. Unfortunately the great expectations connected with the above discovery have not been fulfilled in practice, since the epithelium thus formed is less durable.

J. L. RÉVERDIN first made the experiments in question (*Soc. de Chir.*, Dec. 13th, 1869 ; *Gaz. d. hôp.*, 1870, No. 4, 1871 ; No. 151 ; *Compt.-rend.*, 1871, LXXIII., p. 1280 ; *Arch. gén.*, 1872, XIX., pp. 276, 555, et 703). Concerning the numerous remaining publications, see WEISS (*Ueber Transplant. gänzlich abgetr. Hautstücke*, *Tüb. Diss.*, 1872). On the general pathological conditions, consult FIDDES, *Lancet*, Dec., 1870.—PAGE, *Med. Journ.*, Dec. 3d, 1870.—STEELE, *Ib.*, Dec. 10th, 1870.-JACENKO. *Wien. med. Jahrb.*, 1871, p. 416.—TH. BRYANT, *Guy's Hosp. Rep.*, 1872, XVII., p. 237.—THIERFELDER, *Arch. d. Heilk.*, 1872, XIII., p. 524.—BIESIADECKI, *Unters.*, 1872, p. 60.

According to RÉVERDIN (*Compt.-rend.*, l. c.), transplanted pieces of skin never consist of epidermis alone, but always also of a portion of cutis. In the white man transplanted flaps of skin from other white men, from negroes, rabbits, in the rabbit

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those from rabbits, man and cats succeed. If a transplantation is successful, the piece of skin (*la greffe épidermique*) after twenty-four hours has adhered, is swollen and wrinkled. On the third day there is formed about it a smooth red ring, and the piece now lies buried beneath the summit of the granulations. On the following day the red ring becomes gray, and by degrees whitish; cicatrization proceeds in the same manner. If the pieces have been taken from a pigmented skin (negro, black cats), they gradually become discolored and finally become white. The microscope shows the cells of the epidermis of the piece, at the end of twenty-four hours, in a state of desquamation: the nuclei show RANVIER's vesicular change. On the limits of the flap the epidermis is extended only a little over the granulations; but, besides, it penetrates between the derma and the granulations, and at this points always sends off a more or less deeply penetrating process. The processes going out from the epidermis are always in intimate connection with the embryonic tissue of the wound. In a piece six days old, the surrounding epidermoidal process, found in the depth of the wound, is strongly developed. From the upper border of the piece there extends a layer of epidermis of varying thickness. New and often very voluminous and irregular buds grow out from their deep surface, which penetrate into the embryonic tissue. Globules of epidermis like those in cancroids are often found at its base. On the border the epidermoidal layer extends and divides, becoming, as it were, fan-shaped. This consists of new-formed epidermoidal cells. The connective tissue base of the piece is, after six days, pierced by embryonic vessels, which communicate with those of the granulations, and the connective tissue now shows especially the embryonic character of granulation tissue. Hence R. concludes: 1, the attachment of the transplanted piece occurs in the first place through the epidermis, and only secondarily through the connective-tissue base; 2, the epidermis exercises a kind of action by contact, by which it induces a metamorphosis of the bordering embryonic surface into epidermis.

After the now common transplantations of pieces of skin, the skin retains its vitality for eight hours, and even longer.

JACENKO showed that in transplantations of separated pieces of skin, the cells of the rete Malpighi continue to live on the new base, and may serve as the point of departure of a new-formation: they show increase of nuclei, etc. The connective tissue of a transplanted piece of skin was, on the fifth day, very abundantly occupied at points by young cells; the spindle-shaped cells sometimes showed constrictions, and some of them were multi-nuclear.

That the formation of islands about small particles of skin depends upon a proliferation of the cells of those particles, is seen macroscopically in transplanted black particles of skin: such a particle, in ten weeks, is twenty-fold enlarged, and has sent out its black processes.

HEIBERG (*Med. Ctrlbl.*, 1872, No. 12) successfully inoculated pieces from the wall of an atheromatous cyst upon an ulcer of the leg. CZERNY (*Med. Ctrlbl.*, 1871, No. 17) inoculated epithelium of mucous membrane (uvula) and ciliated epithelium (from nasal polypi) on granulating surfaces of wounds with favorable results. But in both cases the descendants of those cells were later separated from the borders of the cicatrix.

According to some observations, diseases also are conveyed by transplantation (small-pox—pyæmia, syphilis).

That cicatrices, after transplantation of skin on ulcers, offer a greater resistance, is by experience thus far made very doubtful: STUDENSKY, *Med. Ctrlbl.*, 1873, No. 13; oral communications by THIERSCH.

REGENERATION OF LAMINATED EPITHELIUM OF MUCOUS MEMBRANES occurs in the same manner as that of epithelium of the skin; that of uni-laminar epithelium of mucous membranes is in its histological processes still imperfectly known.

PHYSIOLOGICALLY, a throwing off of the greatest part of the epithelium of the body of the uterus, and a quick regeneration of it, occurs at each menstruation. On the conditions in pregnancy, *vide infra*.

In epithelial regeneration with uni-laminar epithelium, either new epithelia arise from the old, on the border; or they proceed from cells similar to lymph-corpuscles, which cells lie under and between the lower and smaller extremities of the cylindrical epithelia (repair-cells (*Ersatzzellen*) of EBSTEIN).

The DERMOID METAMORPHOSIS of portions of mucous membrane, which are exposed to the air, continued irritation, etc., belong in part here : the pavement epithelium on the surface becomes like epidermis, but, according to many, represents only the stratum lucidum ; the cylindrical epithelium is metamorphosed into pavement epithelium (*e.g.*, in the nose, on the eyelids, in the vagina and rectum, on many polypi of mucous membranes), after grafting of cylindrical epithelium on wounds of the skin. The same metamorphosis of many mucous membranes after long-continued chronic catarrhs, sometimes with thickening of the epithelium and new-formation of papillæ, may in part also be included here.

The same is true of the TRANSPLANTATIONS, which consist in separating a portion of the body (in practical surgery a piece of skin) from the body and transporting it to another wounded part. The part to be transplanted remains partly attached to its original site by a vascular bridge, or it is wholly separated from it. The former is the case in plastic surgery.

REGENERATION OF THE NAILS

takes place, if the nails have been destroyed by mechanical injury, burning, freezing, inflammation, or hæmorrhage, of the bed of the nail.

Rarely this regeneration is regularly repeated : according to PECHLIN, a boy every autumn lost his nails, which had become bluish black, together with the epidermis, and again they were renewed. In such cases, according to LAUTH and HYRTL, the whole bed of the nail is covered with soft corneal scales, which by degrees harden, are formed into a true nail and appear with the free border above the points of the fingers (KÖLLIKER, *Hdb. d. Gew.*). New-formation of nails on the second phalanx after loss of the third, was seen by myself in a boy, whose last phalanges of the three middle fingers of the right hand had been cut off : on each of the anterior ends of the three stumps there was formed a small, thick, irregular four-cornered nail.

REGENERATION OF HAIR

takes place, if their bulb is preserved.

According to PINCUS (*Arch. f. Anat. u. Phys.*, 1871, p. 55), the daily fall of hair in middle age averages 55–60 hairs, in children 90, in old age 120.

The hairs, which fall out after severe diseases are, as is well known, regenerated : probably they are formed in the old hair-follicles, since according to E. H. WEBER, the follicles of lost hairs are preserved for a long time. A new-formation of hair in the deeper cicatrices of the skin has not yet been observed.

REGENERATION OF THE TISSUE OF THE CRYSTALLINE LENS

has in some cases from the epithelium of the capsule been with certainty demonstrated.

REGENERATION OF GLAND-CELLS

in particular has not yet been certainly demonstrated, but with respect to some glands (mucous glands, kidneys) is very probable.

The question, whether in deep losses of substance of the skin the sebaceous and sweat-glands are regenerated, has as yet not been definitely answered. The same is true of the glands of mucous membranes in ulcers, etc. A regeneration of gland-cells in the epithelia of the urinary tubules, *e.g.*, in so-called acute Bright's disease after scarlet fever is most probable. Here for days and weeks large quantities of the epithelia of the urinary tubules and casts may be evacuated with the urine, without a subsequent visible effect on the health. According to A. KEY (*Hygeia*, 1869, XXX., p. 530), epithelial regeneration here takes place from the migrated white blood-corpuscles. According to WALDEYER, KLEBS and ZENKER (*D. Arch. f. klin. Med.*,

1872, X., p. 166), similar conditions sometimes occur in acute yellow atrophy of the liver.

B. New-formation of epithelium alone as hypertrophy and as tumor: so-called epithelioma.

Common and tumorous hypertrophies, or hyperplasiæ of epithelium alone occur not infrequently, and with manifold transitions into one another. The longest known are those in the skin, where they are also purest, *i.e.*, without combination with other tissues, and where a number of them are consequent upon oft-repeated irritations of the portion of skin affected.

The mode of origin of epithelia in cases belonging here is not yet known. And yet there occur in the middle, more rarely in the deeper layers of the epithelium, some-times remarkably large cells, those with two nuclei, and with even still further pro-cesses of division. (Observations by EBERTH, RANVIER, GROHE, WALDEYER, and the author.)

Hypertrophy of the epidermis

is met with as indurations or CALLUS, as CORNS or CLAVUS, as ICHTHYOSIS and HYSTRICISMUS, and as many forms of cutaneous HORN, CORNU CUTANE-UM; in part also as WARTS (epithelioma papillare). (On the latter see p. 393.)

The so-called VERRUCA NECROGENICA, which occurs on the hands of anatomists and their assistants, and is distinguished by its wart-like appearance, its chronicity and resistance to means of cure, is, according to WILKS, purely epidermoidal in nature. (See p. 369.)

LEBERT (*Ueber Keratose*, 1864) distinguishes:

I. KERATOSIS CIRCUMSCRIPTA. 1. K. C. epidermica: the horny formation is situated on the free surface of the epidermis. 2. K. C. follicularis: the horny formation pro-ceeds from the cutaneous glands. Varieties of both are furnished by the cornuta (true epidermoidal horny formation) and the multiple non-cornuta (wherein one or many parts of the body are covered with irregular growths of horny substance). II. KERATOSIS DIFFUSA. 1. K. D. follicularis: larger regions of the body, even the whole body, are covered by horny forms, which in adults commonly proceed from the sebace-ous glands, but in the fœtus also from the sweat-glands and hair-follicles. 2. K. D. epidermica (ichthyosis, hystricismus of the authors): the horny growth proceeds especially from the epidermis proper and the stratum Malpighi, but the sebaceous glands, sweat glands and hair-follicles also share in it. Varieties of both diffuse keratoses are: K. lævis (a smoother, uniform thickening), K. rugosa (a more irregular, constantly separating, with rough, fissured surface), and the K. luxurians (of luxuri-ous growth with very large, very differently shaped horny scales). The diffuse kera-toses are either intra-uterine, congenital or extra-uterine, acquired.

HARPECK (*Reich.'s und Dubois' Arch.*, 1862, p. 393) describes the skin of a calf born with ICHTHYOSIS CORNEA.

A considerable thickening of the stratum lucidum is met with in the first stage of epithelial cancer, in papillomata, and condylomata; on mucous membranes, which are dried by the atmospheric air (SCHRÖN, *H. Morg.*, VII., 1865). I find them under many other conditions, where a stronger pressure is exerted on the neighbor-ing structures (epithelial hæmorrhages, healing variola, etc.). Clavus, according to SCHRÖN is an excessive development of the stratum lucidum with consecutive atrophy of the sweat-glands and epidermis; in its vicinity is found hypertrophy of the papillæ, enlargement of the sweat-glands and thickening of the epidermis. By the covering of this epidermis over the callus, the latter may be buried into the cutis.

According to BEIGEL (*Virch. Arch.*, 1868, XLIV., p. 418) ABNORMAL DEVELOP-MENT OF HAIR is found in man, under three forms: 1. the hairs already long in the normal state become extraordinarily long; 2. hairs more or less long are developed in certain parts of the body of persons, on whom in these parts there grows normally only down (beard in children and women, etc.); 3. the down scarcely visible in the

normal state is developed into more or less long hairs : so-called hypertrichosis uni versalis. A true hyperplasia of hairs is found in hairy mother's marks (RIND-FLEISCH).

HYPERTROPHY OF THE EPITHELIUM OF MUCOUS MEMBRANES

occurs as thickening of the epithelial layer of some mucous membranes with multilaminar pavement epithelium (filiform papillæ of the tongue, other parts of the mucous membrane of the mouth, vocal cords, urinary bladder), sometimes simultaneously with the same thickening of the epithelium of the skin.

HYPERTROPHY OF GLAND-CELLS

occurs partly as common increase of size (hypertrophy proper), partly as increase of number (so-called hyperplasia). Both conditions occur sometimes singly, sometimes by side of one another in the same gland. Accurate histological investigations are wanting.

In the GLANDS OF THE SKIN, it is found in so-called milium and in atheroma, also in form of so-called epidermis-pearls, *i.e.*, accumulations of concentrically arranged epithelia in dilated glands or hair-follicles.

An hypertrophy of MUCOUS GLANDS, which consists in enlargement of the old acini and the formation of new ones, occurs sometimes with chronic catarrh of the mucous membranes, so that the excretory gland-ducts and the glands themselves become larger. Sometimes it is found with simultaneous colloid metamorphosis of the gland-cells, as in the upper and under lips ; it forms simple or compound tumors, of the size of a pea to that of a walnut. The so-called hypertrophy of the mucous glands of the soft palate probably also belong here : the tumors reach the size of a walnut to that of a hen's egg.

An hypertrophy of the saccular glands of the stomach and intestinal canal occurs in many cases of chronic catarrh, especially with simultaneous dilatation and elongation of the stomach and intestine.

See the exquisite case by BARTH (*Arch. d. Heilk.*, XI., p. 119).

In the LIVER, hypertrophy of the cells of some lobules is found sometimes in the vicinity of cicatrices, etc., thus as it were compensatory ; general after mechanical hyperæmia, in leucocythæmia, diabetes, without known cause.

In the KIDNEYS, it occurs on both sides in habitual drunkards, diabetics, on one side from arrested function, in or loss of the other kidney.

According to PERL (*Virch. Arch.*, 1872, LVI., p. 305), in the physiological growth of the kidneys most of the formed elements important with respect to function do not increase, the physiological growth is essentially after the type of the hyperplasiæ. In compensatory hypertrophy of the kidneys, however, there is found a true hypertrophy and a more or less considerable dilatation of the spiral urinary tubuli with increase in size of their epithelium ; the straight tubes and their epithelium do not increase in size, the Malpighian bodies not demonstrably so. Probably connected with this true hypertrophy is also a new-formation of glandular tissue and bloodvessels.

2. NEW-FORMATION OF EPITHELIUM AND OF VASCULAR CONNECTIVE TISSUE AT THE SAME TIME.

The new-formation of epithelium and (for the most part) of vascular connective tissue at the same time, occurs under very different forms :

sometimes as regeneration of wounded skin and mucous membranes, some-
times as hypertrophy, sometimes in form of circumscribed or diffuse tumors,
which either remain local or become metastatic.   The epithelium and con-
nective tissue show in the various new-formations the most manifold pro-
portions: for the most part the former preponderates over the latter in
high degree.   The epithelium is therein probably always first present, the
connective tissue new-formation and the for the most part simultaneously
present new-formation of vessels are secondary.

New-formation of skin

occurs : as regeneration of it after wounds and losses of substance chiefly
(see healing of wounds : p. 377); in various diseases of the skin as so-called
hypertrophy (elephantiasis, soft warts or nævus, tumor of the folds of the
skin); very rarely on mucous membranes (so-called dermoid metamorpho-
sis—see p. 467); in dermoid cysts (*vide infra*).

New-formed skin sometimes shows the same layers as normal skin : epidermis,
rete Malpighi, corium (with the so-called pars papillaris and the pars reticularis) and
subcutaneous cellular tissue, usually with the panniculus adiposus.   But at other
times, a so strict separation at least of the deeper layers does not occur.   The vas-
cular papillæ are regenerated from the papillæ of the skin.   After deep injuries of
the skin the cicatrix remains without pigment and papillæ (without glands and
hairs).

Thiersch found the upper limiting surface of the granulations in chronic ulcers of
the leg, translucent, poor in cells, non-vascular, the cell-nuclei elongated, the inter-
cellular substance fibrous.   From that transparent layer proceeds the hyaline limit-
ing membrane, which separates the young epithelium of the vascular stroma.   The
re-formation of cutaneous papillæ Th. derives from the mode of origin and history
of the vessels of the granulations : in the granulation-tissue some perpendicular
vessels are more strongly developed and these persist, while those of weaker devel-
opment, lying obliquely or horizontally, likewise undergo atrophy with the disappear-
ance of the rest of the granulation-tissue.

New-formation of mucous membrane

occurs under similar conditions as that of the skin.   A complete regenera-
tion of destroyed-portions of mucous membrane (by injury, ulceration, etc.)
probably does not take place.

Physiologically, the changes of the uterine mucous membrane during menstru-
ation and pregnancy are worthy of note.   During menstruation the mucous mem-
brane really increases, thickens to the extent of from 2 to 4, even 6 mm., in its
prominent folds from 10 to 12 mm., becomes softer and shows, besides the strongly-
developed glands, many young, round, and spindle-shaped cells in its tissue (Kölli-
ker).

On the question, whether after birth the remains of the decidua remain or not on
the inner surface of the body of the uterus, there have been for a long time two oppo-
site views : the one is represented by W. Hunter (*Anat. Descr. of the Hum. Grav.
Uterus*, 1769), Virchow (*Verh. d. Geburtsh. Ges. zu Berlin*, 1847. III., p. XVII.).
Colin (*Ét. sur la surf. int. de l'utérus après l'accouchement*, 1847), Coste, Robin and
others ; the other by Cruveilhier (*Anat. pathol.*, Livr. XIII.), Arnold, Heschl,
Kölliker and others.   According to Friedländer (*Physiol.-anat. Unters. üb.
d. Uterus*, 1870), the decidua at the end of pregnancy consists of two layers, an in-
ternal cellular layer, the essential nature of which is that of connective tissue,
and an external glandular layer.   By the separation of the decidua during birth only
the internal portion of the cellular layer is removed, its external layer, besides the
whole glandular layer, remains after birth in the uterus.   Very soon after birth the
portions of the cellular layer remaining behind are destroyed by fatty degeneration,
the glands thereby become free, open, and sometimes unite, especially through
fatty destruction of the intermediate connective tissue, thereby forming a continuous

epithelial covering over the whole inner surface of the uterus. In place of the destroyed connective tissue elements, young forms arise through active growth.

The so-called DYSMENORRHŒA MEMBRANACEA consists in this, that in menstruation the mucous membrane is thrown off, comes with the menstrual blood to the exterior, and is completely regenerated by the time of the next menstruation. According to HAUSMANN (*Mschr. f. Geburtsk.*, 1868, XXXI., p. 1), this process, until now regarded as disturbance of menstruation, is always the result of sexual intercourse and never occurs in maidens. It is an abortion of the first days and weeks, in which after the destruction or passing away of the fœtus, the uterine mucous membrane metamorphosed into decidua, is thrown off with pains. The abortion appears preferably at time of menstruation. HEGAR and MAIER (*Virch. Arch.*, 1871, LII., p. 161) dispute this view.

NEW-FORMATION OF DENTINE

occurs in various forms in normal teeth, also as supernumerary teeth of the alveoli and in many dermoid cysts.

According to WEDL (*Wbl. d. Ztschr. d. Wien. Aerzte.* 1863, No. 52), new layers of dentine are formed on the internal surface of the dentine until late in life.

Very rarely broken teeth heal by formation of callus. In the callus, dentine is found near the surface of fracture, dentine as a central layer and globular masses of varying size here and there distributed in it (WEDL).

MITSCHERLICH (*Arch. f. klin. Chir.*, 1863, IV., p. 375) has practised re-plantation, as well as transplantation of teeth of the living and of dead teeth. In some cases there probably occurs a true healing of a re- or transplanted tooth, so that new vessels and nerves really penetrate into the tooth. Healing for the most part succeeds only when the periosteum of the alveolus is wholly or nearly entirely preserved. The periosteum by constant pressure seems to effect a partial resorption of the tooth, and, by the deposit of bony masses from the swollen soft substance, the tooth is made fast.

From tumors proper of the teeth, DENTAL OSTEOMATA, are to be sharply defined retained teeth and tumors, which are developed from the surrounding bones, either from the alveolus (ALVEOLAR EXOSTOSES), or from the interior of the bone as well as especially in teeth retained deeply in the alveolus. Dental osteoma proceeds, either from a formation of new cementum from the membrane of the root, and then covers the roots to a large extent, or forms small exostoses (dental exostosis in the narrower sense); or it is represented for the most part by small, globular or hemispherical, enamel-covered hyperplasiæ of the crown, neck or root (*dentes proliferi*); or there is blending of the teeth with each other, sometimes throughout, sometimes only at points; or it exists as ODONTOMA, *i.e.*, formed from dentine proper. (VIRCHOW, *Die krkh. Geschw.*, II., p. 53.) Consult also ALBRECHT, *Klin. de Mundkrankh.* 2. H. 1872, p. 1.

NEW-FORMATION OF SKIN WITH SEBACEOUS AND SWEAT-GLANDS.

A complete REGENERATION has not yet been certainly observed, but seems to be possible if only the uppermost portions of these glands lying in the epithelium has been destroyed.

HYPERTROPHIES OF THE SKIN and of the sebaceous and sweat-glands occur in some cutaneous diseases.

An enlargement of sweat-glands, especially a dilatation of their lumen, has not infrequently been observed, *e.g.*, in elephantiasis Græcorum, in many soft warts. The same enlargement of the glandular pouch with fatty degeneration of the glandular epithelium (as well as the latter without enlargement), has its origin, according to VIRCHOW, in the copious sweating of those affected with, *e.g.*, phthisis.

New-formation of SKIN with sebaceous and sweat-glands, rarely only with the latter, occurs in the wall of many cysts (see Dermoid cysts).

NEW-FORMATION OF MUCOUS MEMBRANE AND OF ITS GLANDS.

REGENERATION is not certainly known.

TUMOROUS HYPERTROPHY forms the so-called MUCOUS POLYPI of most mucous membranes.

NEW-FORMATION OF GLANDULAR TISSUE.

HESCHL, *Ztschr. d. Ges. d. Wien. Aerzte*, 1852.—ROKITANSKY, *Sitzungsber. d. Wien. Acad.*, 1853; *Ztschr. d. Ges. d. Wien. Aerzte*, 1860.—BIRKETT, *Guy's Hosp. Rep.*, 1855.—ROBIN, *Gaz. méd. de Paris*, 1855.—E. WAGNER, *Schmidt's Jahrb.*, 1859, CIII., p. 92; *Arch. d. Heilk.*, II., p. 473; XI., p. 44.

REGENERATION of glandular tissue (cells and stroma) is not yet known.

HYPERTROPHY, or HYPERPLASIA of GLANDULAR TISSUE, or of whole glands, consists either only in an enlargement, or also in an increase of the gland-cells (see p. 469); or, at the same time, also in a proportional increase of the vascular stroma of the glands, in such manner that the new-formed glandular tissue agrees essentially with the normal, and has the same function. PHYSIOLOGICALLY this process is met with in the development, and especially in the so-called hypertrophy from lactation of the lacteal glands during pregnancy. In the OVARIES there occurs, in the physiological state, a continuous new-formation of the so-called Graafian follicles until the climacteric period. PATHOLOGICALLY, a similar hypertrophy takes place in the mamma, sometimes during uterine disease, and under unknown conditions. Also here belong the not yet accurately histologically investigated cases of so-called hypertrophy of one organ in atrophy or consumption of the other, hypertrophy of the left lobe of the liver in atrophy of the right, hypertrophy of single acini, perhaps even new-formation of these in the vicinity of cicatrices. (See also p. 469.)

In the absence, congenital or acquired, of one kidney, the other is found almost always more or less enlarged. The investigations relative to this, of VALENTIN, ROKITANSKY, BECKMANN, and others, recently of ROSENSTEIN (*Virch. Arch.*, 1871, LIII., p. 141), have afforded no determined results on the histological character of such kidneys. The increase of function of enlarged kidneys acts in a wholly compensatory manner, as well with respect to the excretion of urine as to that of urea.—See also RAYER, *Tr. d. mal. d. reins.*, III., p. 762. SIMON, *Chirurgie der Nieren*, 1872.

TUMOROUS NEW-FORMATION OF GLANDULAR TISSUE, ADENOMA.

ADENOMA forms sharply, and usually, as it were, encapsuled, defined knots of varying size, rarely partially connected with the original organ, and, according to the kind of gland, of varying color, consistence, etc., and which for the most part penetrate the surrounding textures, and more rarely partly supplant them. The glandular tissue rarely forms a subordinate, usually the chief element.

The GENESIS of new-formed glandular tissue is in most cases the same as that of the normal. Sometimes there takes place only an enlargement of the gland-cells and the smallest divisions (follicles, acini, etc.). At other times, the gland-cells increase by repeated division: thereby either the smallest division of the gland becomes uniformly larger; or there arise bud-like, at first solid out-growths or processes, which grow into the surrounding connective tissue, again to form new growths, and often at the same time to ramify. These processes sometimes later become hollow, and thus receive a gland-like lumen, but more often they continue solid. In their periphery they are sometimes covered with a tunica propria. (Like the glandular epithelium, so also probably may the epithelium of the affected skin or mucous membrane project adenomata into the corium by

growth of its lowest epithelia.) Connective tissue and vessels are developed in a corresponding proportion to the normal organ. Later, these tumors remain in connection with the old gland; or they are completely isolated from it. The latter takes place, sometimes through independent atrophy of some parts, sometimes through the simultaneous growth in the usual way of the surrounding connective tissue.

Many assume also a new-formation of glandular tissue from connective tissue. The connective-tissue corpuscles in the vicinity of the glands divide, and the indifferent round cells thus arising are metamorphosed partly into epithelial, or glandular cells, with their characteristic arrangement, partly into connective tissue.

The FUNCTION of new-formed glandular tissue rarely agrees perfectly with that of the normal glands: it for the most part has no function. This is especially true of probably all tumorous adenomata, which, with the mother-tissue and bordering tissues, behave like other tumors. They are of themselves benign new-formations, which after complete extirpation, for the most part do not return. But many have a tendency to pass into cancerous forms.

The cases of glandular new-formation, which depend on the foetal period, as the thymus gland, *lienes accessorii*, supra-renal capsules, the occurrence of hepatic substance within the liver (ROKITANSKY, *Wien. allg. med. Ztschr.*, 1859, p. 98), as well as in the *ligamentum suspensorium* (the author, *Arch. d. Heilk.*, II., p. 471), etc., do not belong here. With respect to most adenomata, it is undetermined whether they originate during the foetal period and are further developed only at a later age.

The group of the adenomata is less sharply defined than that of most other new-formations. There exist not only manifold transitions between glandular hypertrophies and glandular tumors, but the former are often with difficulty distinguished from many inflammatory swellings, and the latter not infrequently show transition-forms to epithelial cancer.

The anatomical and histological structure of adenomata is often determined with difficulty, not only on account of the above-mentioned transition-forms, but also on account of the CHANGES not infrequently occurring in them, or in the neighboring structures. These consist in disturbances of the circulation, especially hæmorrhages and œdema, in metamorphoses, like the fatty, mucous, and especially the colloid, as well as in new-formations of papillary connective tissue, which grow from the neighboring structures into the new-formed glandular tissue, and thereby may produce the most confused macroscopical and microscopical forms, which hardly permit the forming of a conclusion. Finally, new-formed glandular tissue shows an especial tendency to cyst-formation.

General, as well as partial tumorous glandular new-formations, have been observed especially in the compound racemose glands, most often in the female mammæ, as well as in the prostate and thyroid glands, adenomata, especially in the skin and in the mucous membranes.

ADENOMATA OF THE SKIN

form diffuse or circumscribed tumors, of a size varying to that of an egg and larger, over which the skin is at first but little changed, but later is often ulcerated: ADENOMA SUDORIPARUM and AD. SEBACEUM. In both cases, they consist of glandular pouches, whose size, ramification, epithelium, etc., makes their origin from sweat-, or sebaceous glands probable, and from the varying (in quantity) intermediate vascular connective tissue.

REMAK, *Deutsche Klin.*, 1854, No. 16.—FÖRSTER, *Atl. d. p. Anat.*, Taf. XXIII.,
Figs. 1–4.—LOTZBECK, *Virch. Arch.*, XVI., p. 160.—VERNEUIL, *Arch. gén.*, 1854, p.
447.—THIERFELDER, *Arch. d. Heilk.*, XI., p. 401.
(On RINDFLEISCH's view, that lupus is an adenoma of the sebaceous and sweat-glands, see p. 438.)

ADENOMATA OF MUCOUS MEMBRANES

occur partly as hypertrophies of the glands of mucous membranes, which in
many cases form sharply circumscribed cyst-like tumors (see p. 469) ; in
part they are found simultaneously with stronger new-formation of vascular
connective tissue in form of the so-called MUCOUS POLYPI.

MUCOUS POLYPI are for the most part broad, rarely small pedicled, round
or oval, simple or irregular, lobed, etc., forms of a size varying from that of
a bean to that of a hen's egg and larger, whose surface on the whole resem-
bles that of the mucous membrane, and affords for the most part a distinct
mucous character, while the cut surface is of a more or less fibrous texture,
and is commonly rich in blood.   These tumors owe their names to the
mucous glands found on their surface and within, and to a large extent
opening on the former.   The latter are found in varying, for the most part
large numbers ; they are more rarely simple, more often compound, pouched,
and irregularly racemose, essentially similar to the normal mucous glands.
The surface of the polypi is generally covered with the same epithelium,
which belongs to the mucous membrane ; on the polypi, or parts of them
lying externally (aural and rectal polypi), it becomes lamellar.   The mass
of the polypi consists for the most part of very vascular, sometimes nerve-
bearing connective tissue, which on the surface not infrequently forms
numerous papillæ.   The interior of the polypi shows, besides the glands,
almost constantly various numerous, for the most part small, round, serous
or mucous cysts, sometimes so extended that the polyp loses its glandular or
mucous character, and becomes a so-called CYSTIC or VESICULAR POLYPUS.

The glands of mucous polypi arise by a turning in of the epithelium of the sur-
face of the polypus, as is the case in similar glands in the embryo and in childhood.
Their enlargement takes place in the same manner by turning out, etc., of the at
first pouch-like fôrms.   Many polypi of the gastric mucous membrane depend upon an
elongation and dilatation of the peptic glands (FÖRSTER).

Mucous polypi occur on almost all mucous membranes : most often in the
nasal, naso-pharyngeal cavities, rectum, and uterus.
The CONSEQUENCES of MUCOUS POLYPI depend especially upon their
volume, and upon their relations with the canal lined by the mucous mem-
brane, upon their position and the possibility of a change of position
(especially with polypi with small pedicles), upon their nearness to the
surface of the body, upon their vascularity, upon the changes of their
parenchyma, upon the irritation which they exercise on the affected mu-
cous membrane.   Polypi are therefore sometimes entirely devoid of symp-
toms (small or of medium size, even very large polypi in large channels
lined by mucous membrane, *e.g.*, the stomach) ; sometimes they give rise
to lasting or transient contractions and obstructions of the channel (espe-
cially polypi of the mucous membrane of the air-passages), which under vari-
ous circumstances are increased or diminished (damp weather, exacerbations
of catarrh of the mucous membrane, etc.).   If they are situated near the
surface of the body on a movable mucous membrane, they appear from time
to time or are always present on the former, give rise to tenesmus and
similar sensations, prolapsus of the mucous membrane ; under the same

conditions, or also spontaneously, they give rise to hæmorrhages of varying importance, even endangering health and life. Almost all keep up chronic catarrhs of the affected mucous membrane, which, after removal of the polypi, for the most part quickly disappear, and in consequence of it there are frequently formed hypertrophies of the mucous membrane alone or of the whole organ.

BILLROTH, *Ueb. d. Bau d. Schleimpolypen.*, 1855.

ADENOMATA OF COMPOUND RACEMOSE GLANDS,

especially of the mamma and parotid, form tumors of varying size, for the most part circumscribed, rounded, and usually easily enucleated. They consist of rounded or elongated bodies, like vesicular glands, but for the most part, larger and more irregularly formed, with a peripheral homogeneous membrane and nucleated cells on their internal surface arranged like epithelium, with or without a central space, indicated as a gland-lumen. These vesicular glands, for the most part arranged in groups, lie in a soft proportionately abundant connective tissue ; they however are, for the most part connected by new-formed ducts, and are not in demonstrable connection with the mother-gland. In general these tumors are grayish-red or dark red, fleshy and glandular, and permeated by connective tissue cords variously arranged, with scanty or abundant, mostly mucous juice. The further gross anatomical properties vary in a manifold manner, according as the tumor takes possession of only one or several lobes of the glands or their whole extent (partial and general glandular tumor), according to size, form, connection, etc., of the new-formed vesicular glands, according to their further metamorphoses (cyst-formation, tuberculization, etc.), according to their number (pure or fibroid glandular tumor) and kind (fibrous tissue or mucous or cartilaginous or sarcomatous tissue) of the new-formed tissue serving as stroma, according to the behavior of the fatty tissue, which sometimes increases greatly, according to the behavior of the gland-ducts (often dilatation of them, sometimes transformation into cyst-like spaces and the origin of papillary and other growths of varying structure on their internal surface : cysto-sarcoma simplex, phyllodes, proliferum, etc.).

A similar hypertrophy affecting all or only a portion of the glands occurs in rare cases also in the PANCREAS. BECKER (*Œstr. Jahrb.*, 1867, p. 17) describes in full detail an adenoma of the lachrymal glands.

A cystomatous adenoma of the pituitary body of the size of a walnut was observed by W. MÜLLER (*Beob. d. path. Inst. zu Jena*, 1871, p. 425).

ADENOMATA OF THE PROSTATE GLAND

consists sometimes in a general, sometimes, especially in advanced age, also in a partial hypertrophy. The latter is represented as a new-formation of for the most part sharply circumscribed and easily enucleated, broad or polypous tumors of a varying size, to that of a cherry and larger, lying in the interior of the gland or on its surface, in the latter case especially frequent in the cavity of the bladder. These have a structure quite analogous to that of the normal prostate, but without connection with its excretory ducts : the glandular tissue shows in comparison with the connective or muscular tissue a for the most part only scanty increase. Like the normal gland, they often become the seat of the development of amyloid and colloid bodies and so-called prostatic concretions. Glandular tumor of the prostate, in its larger volume and unfavorable location, is followed by

stricture of the neck of the bladder, and thereby catarrh of the mucous membrane, hypertrophy of the muscular coat, etc.

ADENOMATA OF THE LIVER

occur in two different forms : in both are found pale brown and soft knots, which vary in size, are very small (miliary) or reach a diameter of 5 cent., separable from the surrounding tissues and compressing them, which knots not infrequently occur singly or in small numbers, and are accidentally found after death from other causes, while they are more numerous in other and rarer cases, behave like cancer of the liver, and are the essential cause of death. The first form is probably congenital or has already existed for a long time, while the latter is of more recent date and still shows processes of growth.

According to RINDFLEISCH and others, the process of formation is as follows : the hepatic cells of a part become curved, and thus form a globular space, and then push forward shoots. The new-formed cells often become cylindrical and are arranged after the manner of compound saccular glands, with or without lumen. About the tumor there then arises a connective tissue envelope. The surrounding hepatic tissue is compressed. The adenomata may later undergo fatty degeneration, their capsule may suppurate, etc.

GRIESINGER and RINDFLEISCH, *Arch. d. Heilk.*, V., p. 385 et 395.—FRIEDREICH, *Virch. Arch.*, XXXIII., p. 48.—EBERTH, *Ib.*, XLIII., p. 1.—WILLIGK, *Ib.*, LI., p. 208 (assumes the origin of hepatic adenomata from colorless blood-corpuscles)

HYPERTROPHIES AND ADENOMATA OF THE THYROID GLAND

occur in many forms : 1, as dilatation of the original glandular vesicles, which affects the whole thyroid gland uniformly or some lobules chiefly, for the most part with colloid degeneration (so-called SIMPLE GOITRE) ; 2, as new-formation of glandular elements, increase of glandular follicles (so-called HYPERTROPHIC GOITRE), occurring for the most part simultaneously with the first form. There arise rounded tumors (so-called goitrous knots) from the size of a pea to that of a walnut and larger, which are separated by a connective tissue capsule from the normal gland and may finally induce atrophy even in these ; development of new rounded thyroid gland bodies of the size of a pea, bean or hazel-nut near the thyroid gland (accessory glands)—probably for the most part congenital. The new-formation of all these forms proceeds from the glandular epithelium. This grows at one point and forms a protrusion of the gland-membrane, which gradually becomes larger and then is separated by constriction.

Two cases of congenital adenoma of the thyroid gland are described by W. MÜLLER (l. c., p. 454).

New-formed glandular tissue becomes affected in the same manner, and quite as frequently as the normal : hyperæmia, inflammation, hæmorrhage, colloid, fatty and chalky metamorphoses occur near, and in the new-formed masses, and give rise to very different forms, which often represent the enlarged thyroid gland.

ADENOMATA OF THE TESTICLES, KIDNEYS, ETC.,

also probably occur, but as yet are unknown, or have been confused with epithelial cancers of those organs.

OVARIAN CYSTS and cystoids likewise belong in part to the adenomata : so-called myxoid or colloid cystomata. While, according to many, they arise from connective tissue, others have shown with certainty their epithelial origin. They proceed from the rounded or elongated saccular epithe-

lial masses, which form the processes of the Graafian follicles. They remain in part glandular, in part there arise cysts, through transudation from the bloodvessels and through cell-metamorphosis.

XIII. CANCER OR CARCINOMA.

(Epithelial cancer, and endothelial cancer. Connective-tissue cancer.)

BURNS, *Diss. on Infl.*, 1800, II. ; *Princ. of Surg.*, 1838, I.—ABERNETHY, *Surg. Works*, 1811, II.—BAYLE et CAYOL, art. *Cancer* in *Dict. d. sc. méd.*, 1812.—LENNEC, art. *Encéphaloïde* in *Dict. d. sc. méd.*, 1812.—OTTO, *Seltene Beob.*, 1816, I., p. 119 ; 1824, II., p. 108.—DUPUYTREN, *Consid. génér. sur le cancer*, 1817.—WARDROP, *Obs. on Fung. Hæmat.*, 1809.—MAUNOIR, *Mém. sur les fong. méd. et hémat.*, 1820. —BARING, *Ueb. den Markschwamm des Hodens*, 1833.—SCARPA, *Sullo scirro e sul cancro*, 1821.—CARSWELL, art. *Scirrhus* in *Forbes' Cyc'op. of Pract. Med.*, 1833.— HANNOVER, *Müll.'s Arch. Jhrber. f.* 1843 ; *Das Epithelioma*, 1852.—J. MÜLLER, *Ueb. d. fein. Bau und. die Formen der krkh. Gesche.*, 1838 ; *Arch.*, 1843, p. 438.— ECKER, *Arch. f. phys. Heilk.*, 1844, p. 380.—LEBERT, *Müll's Arch.*, 1844 ; *Phys. path.*, 1845, II. ; *Virch. Arch.*, IV., p. 192 ; *Traité prat. des maladies cancéreuses*, 1851.—MAYOR, *Bull. de la soc. anat.*, 1844, p. 218 ; *Réch. sur. les tum. épiderm.*, 1846.—BIBRA, *Arch. f. phys. Heilk.*, 1846.—ROKITANSKY, *Hdb. d. path. Anat.*, 1846, I. *Ueb. d. Entw. der Krebsgerüste, Sitzungsber. d. Wien. Acad.*, 1852 ; *Ueb. d. Zottenkrebs, Ibid.; Ueb. d. Gallertkrebs, Ibid.*—WALSHE, *Nature and Treatm. of Cancer*, 1846.— BRUCH, *Die Diagnose der bösartigen Geschw.*, 1847 ; *Ztschr. f. rat. Med.*, 1849, VII. ; *Arch. f. phys. Heilk.*, XIV.—REINHARDT. *Virch. Arch.*, 1847, I., p. 528 ; *Ann. d. Char.*, II., p. 1.—BENNETT, *On Cancerous and Cancroid Growths*, 1849.— FRERICHS, *Jenaische Annalen*, 1849.—VIRCHOW, *Würzb. Verh.*, 1850, I., p. 106 ; *Arch.*, I., p. 94 ; III., p. 22 ; XI., p. 89 ; *Gaz. méd. de Paris*, 1855, p. 211.— FÜHRER, *Deutsche klin.*, 1851, No. 34 ; *Virch. Arch.*, IV., p. 584.—BIDDER, *Müll.'s Arch.*, 1852, p. 178.—BROCA, *Mém. de l'acad. franc.*, 1852, XVI.—GERLACH, *Der Zottenkrebs*, 1852.—REDFERN, *Monthly Journ.*, 1850.—REMAK, *Deutsche Klin.*, 1854.— SCHRÖDER VAN DER KOLK, *Nederl. lanc.*, 1853.—E. WAGNER, *Arch. f. phys. Heilk.*, 1858. p. 153 ; 1859, p. 306 ; *Arch. d. Heilk.*, I., p. 157 ; III., p. 143 ; *Der Gebärmutterkrebs*, 1858.—SCHUH, *Prag. Vjschr.*, 1851.—KÖHLER, *Die Krebs- und Scheinkrebskrankh.*, 1853.—DEMME, *Schweiz. Monatschr.*, 1858, III.—FÖRSTER, *Virch. Arch.*, 1858, XIV., p. 91 ; *Würzb. Ztschr.*, IV., p. 317 ; *Hdb. d. path. Anat.*, I., p. 388.—BILLROTH, *Virch. Arch.*, 1860, XVIII., p. 82 ; *Arch. f. klin. Chir.*, VII., p. 860.—EISELT, *Prag. Vjschr.*, 1862, LXX. et LXXVI.—THIERSCH, *Der Epithelialkrebs nam. der Haut.*, 1865.—WALDEYER, *Virch. Arch.*, 1867, XLI., p. 470 ; 1872, LV., p. 67.—KÖSTER, *Die Entw. d. Carcin.*, etc., 1869.
(Consult besides the text-books of pathological anatomy and surgery.)

CANCER is a term applied to a new-formation occurring as a tumor or infiltration in almost all tissues and organs, and which is diffuse, single or multiple, very rarely acute, for the most part chronic, of varying size, form, color, consistence, etc. It consists essentially of CELLS, which in size, form, partly also in arrangement, etc., are like, or similar to other physiological cells (epithelial and gland-cells, endothelial cells, colorless blood corpuscles), but especially through their number and metamorphoses are followed by destruction of affected parts of the organ, and finally, almost always by that of the organ itself. After extirpation cancer usually returns.

The SYNONYMS of CANCER are extraordinarily numerous. They concern least its special forms and metamorphoses (*e.g.*, scirrhus, fibrous cancer, medullary cancer, epithelial cancer, cellular cancer, gelatiniform cancer, alveolar cancer, reticulated cancer, carcinoma melanodes. hæmatodes, etc.) ; for the most part they relate to the various theories on the origin and nature of cancer (*e.g.*, besides a number of the synonyms already given, spongoid inflammation, fungus medullaris, medullary sarcoma, encephaloid, *matière cérébriforme*, milk-like tumor, galactomyces, etc.).

The above definition of cancer is partly pathologico-anatomical, partly clinical. By their essential elements, especially by the form and arrangement of their cells, as well as by the origin of the latter, cancers are distinguished as epithelial cancers, connective-tissue cancers, and endothelial cancers.

EPITHELIAL CANCER, in the broader sense, consists of cells arranged like epithelium in distinct, and for the most part comparatively large alveoli, which cells, with respect to their situation and origin, are more or less similar to those of the epithelium of the skin or of the laminated pavement epithelium, of the cylindrical epithelium, or of the epithelium of many true glands. These cells are immediate descendants of the epithelium of the skin, mucous membranes, or glands ; they arise either by a growth of the elements of these into the surrounding, for the most part connective tissue, textures. Connective-tissue cancer consists of round or rounded, for the most part smaller cells, not arranged like epithelium. These arise from the connective-tissue corpuscles or of the tissues analogous to it.

Epithelial cancer proceeds from forms of the upper and lower germinal layer, and therefore belongs to the series of new-formations of true epithelium, of the formations of adenomata and many cysts. Connective-tissue cancer, on the other hand, arises from forms of the middle germinal layer, especially of common connective tissue, and thus is ranged with the formation of sarcoma, glioma, etc.

Intermediate between epithelial and connective-tissue cancers stands endothelial cancer. In all essential properties it resembles epithelial cancer, but arises from endothelial cells, thus from forms of the middle germinal layer.

Epithelial and endothelial cancers are in general ATYPICAL EPI- and ENDO-THELIAL TUMORS, connective-tissue cancers are ATYPICAL CONNECTIVE-TISSUE TUMORS.

Since with the exception of the kind, arrangement, and origin of the cells, the remaining anatomical and clinical properties of the three chief forms of cancer essentially agree, and since the above division cannot yet be extended to some tumors, and is not accepted by many, we will treat of the general anatomico-pathological and clinical properties of both forms of cancer together.

For the same reasons, as well as on account of the especially conspicuous malignity of cancerous new-formations, we regard cancer as a special form of tumor. Brief mention has already been made of connective-tissue cancer in the consideration of heterologous new-formations of connective tissue (p. 439), of epithelial cancer in that of epithelium (p. 470), of endothelial cancer in that of endothelium (p. 394).

Cancer affects all tissues, with the exception of cartilage, the internal and middle coats of the arteries, and all organs, in very varying frequency. In general, the following ORDER OF FREQUENCY holds good with respect to the SEAT OF CANCER : most often the lymph-glands, female mammæ, uterus with the vagina, lower lip, liver, stomach, œsophagus, serous membranes ; more rarely the lungs, various portions of the skin, intestinal canal, veins and lymphatic vessels, bones, brain and its meninges, eye, kidneys, suprarenal capsules. testicles, tongue ; most rarely the urinary bladder, ovaries, muscles, air-passages, salivary glands, tonsils, thyroid gland, spinal cord, spleen. Besides, cancer shows an especial preference for certain parts of organs : vaginal portion of the uterus, pylorus of the stomach, transition points of skin into mucous membrane, lower extremity of the small intestine, cæcum, rectum, trigonum of the urinary bladder, etc.

The ORDER OF FREQUENCY above given of the occurrence of cancer holds good

only in an absolute sense. With respect to the frequency of the organ attacked by primary and secondary cancer, the scale is about as follows: For PRIMARY cancer: first, the female mamma, lower half of the uterus with the vagina, lower lip, stomach, œsophagus, lymph-glands; then the skin, liver, intestines, bones, urinary bladder, kidneys, brain and meninges, testicle, the eye; last, the ovaries, lungs, air-passages, serous membranes, thyroid gland, salivary glands, lymphatic vessels. For SECOND-ARY cancer: lymph-glands and connective tissue (lymphatic vessels?) in the vicinity of the primary cancer; the affected serous membranes; liver and lungs; skin, muscles, bones, heart; finally, all remaining organs. Most of those organs in which primary cancer is especially frequent, show secondary cancer extremely rarely (mamma, uterus, stomach), while in many organs, as the liver and lymph-glands, both forms of cancer are of not infrequent occurrence.

In organs which exist in pairs (mammæ, kidneys, testicles, lungs, salivary glands, etc.), for the most part only one organ, sometimes later also the other, rarely both simultaneously, or soon after one another, become affected by primary cancer. Secondary cancer occurs for the most part in both organs of a pair.

Cancer not infrequently also occurs in other new-formations, especially of connective tissue (in pseudo-membranes, adhesions and inflammatory thickenings of serous membranes, in the cicatricial masses from gastric ulcers, in many new-formations of the skin, etc.), in cysts, etc. On the metamorphosis of many new-formations into cancer, *vide infra.*

Cancer occurs singly or in great numbers. That is especially true of it, which was said above (p. 365) of primary and secondary or metastatic new-formations. In general, epithelial cancer is followed by secondary cancers, if we except those of the corresponding lymph-glands, more rarely or for the most part in less number than connective-tissue cancer.

Cancer appears either in form of TUMOR or INFILTRATION. The latter is the case in most primary, the former in most secondary cancers.

The CANCER TUMOR (cancer swelling, cancer knots, so-called circumscribed cancer) is of a size varying from that just perceptible (miliary cancer) to that of the head and larger. Its form is regularly round or irregular, knotty, branched, etc. Its consistence varies from that of almost bony hardness to that of pulpy softness: according to the number of proper cancer-cells and the character of the stroma. Hard cancers, without reference to structure, are often called SCIRRHUS; the soft, MEDULLARY. Cancer knots, especially those which are secondary, appear to the naked eye frequently more or less sharply defined; and they can be enucleated, or microscopically they show almost always a continuous connection with the normal tissues. Only in extremely rare cases is the cancer tumor really separated from the surrounding textures by a layer of loose connective tissue (capsule) free from cancer and easily enucleated. The surrounding textures of most cancer knots show a slight compression of the tissues not proportionate to the size of the cancer. Cancer, in form of tumor, is found especially in the interstitial connective tissue of the most various parts, in and beneath the skin and in serous membranes, in the brain, liver, spleen, lungs, etc.

CANCEROUS INFILTRATION (infiltrated or diffuse cancer) occurs most often primarily, in the skin, in mucous membranes and hollow organs (uterus, etc.). The affected skin or organ is then to a greater or less extent so uniformly permeated by a homogeneous, variously colored mass, often yielding a milky juice, that the structure is not at all, or only partly recognizable, and the tissue appears in various degrees thickened.

The ELEMENTS OF CANCER are CANCER-JUICE and a firm substance serving as a reservoir or support, the STROMA.

CANCER-JUICE consists of CANCER-CELLS and a usually scanty, fluid substance, the intercellular substance, or CANCER-SERUM. The CANCER-STROMA

forms, in epithelial and endothelial cancer, more or less numerous, closed or connected cavities, of varying size and form, the so-called ALVEOLI OF CANCER, within which the cancer-cells, at first arranged similarly to glandular cells, are contained; in villous cancer there are, besides, papillary excrescences of varying form, in the periphery of which the cancer-cells lie; in connective tissue cancer an irregular, sometimes narrow, sometimes wider net-work of for the most part scanty connective-tissue fibres, or of the character of reticular connective substance, in the space of which the cancer-cells, single, few, rarely many, are found.

The alveolar structure of cancer was long regarded as especially characteristic. This however is not the case. Adenoma also, and many sarcomata and cystomata, show an alveolar structure. To draw conclusions from the alveolar texture of new-formations, it is almost always necessary to consider the structure of the mother-tissue.

THE CELLS OF CANCER

have no specific characteristics. There are only a few points by which they may with probability be recognized. These are the comparatively considerable NUMBER of cells, their frequently large size, their IRREGULAR SHAPE, which agrees more or less only with a few physiological cells, the frequently multiple nuclei and nucleoli, the for the most part CONSIDERABLE SIZE OF THE NUCLEUS, and also of the nucleolus, the ARRANGEMENT OF THE CELLS DEPARTING more or less from that of those of the textures hitherto described.

A demonstrable INTERCELLULAR SUBSTANCE is wanting in most cancers; some cancer-cells are more or less firmly connected together by a material which is invisible. In many cancers however there is found a clear, liquid, albuminous or mucous substance in for the most part small quantity. It is already present, either in cancers examined in the fresh state, or it appears only when the cancers have been subjected to examination a long time after extirpation or after death. In the latter case, it is formed as an excretion of the cells, or by metamorphosis of the cell-contents, or by destruction of the cells.

MELANOTIC or PIGMENT-CANCER, carcinoma melanodes (malignant melanosis), is distinguished from common cancers by the gray, grayish-brown, brown or deep black coloring of the external or cut surfaces, and by the similarly colored juice. This coloring either affects all cancers of the body, primary and secondary; or clear cancers are found with the dark; or some or all knots are partly of the usual color, partly more or less dark colored. In many cases, cancers operated on at first were of the usual color; each of those operated on later was darker. Melanotic cancers moreover are sometimes connective-tissue cancers, sometimes epithelial. Their primary SEAT is sometimes only those parts in which is found physiological or pathological pigment; most often the eye, the eyelids, the external previously normal skin or skin "marks," or cicatrices resulting from extirpation. Secondary cancers are for the most part very numerous, and sometimes distributed over almost all parts of the body, especially the lymph-glands, liver, lungs, bones and serous membranes.

Microscopical investigation shows, besides various numerous uncolored cancer cells, others with more or less numerous, brown or black, very small molecules or larger granules; often most of the cells decay, so that only free pigment is visible. The stroma is sometimes abundant, sometimes scanty, usually vascular, sometimes color-

less, sometimes in various degrees pigmented. The pigment-granules are distributed uniformly or in larger or smaller, spindle-shaped cavities.

In melanotic cancer the cancer-cells receive the coloring matter chiefly from the nutritive liquid, like the epithelium of the choroid, the conjunctiva, the cells of the rete Malpighi, many ganglion-cells: perhaps in part also from capillary hæmorrhages. According to RINDFLEISCH (l. c., p. 106), a taking up of the dissolved coloring matter of the blood takes place from the blood: he found the first traces of pigmentary infiltration in the endothelium of the vessels.

Melanotic tumors are, according to many, most often sarcomata, according to others, carcinomata. LÜCKE (*D. Z. f. Chir.*, 1873, II., p. 199) regards MELANOMA as a tumor *sui generis*. The pigment-cell is something specific; it can be an epithelial cell, a connective tissue cell: it sometimes produces carcinoma, sometimes sarcoma, sometimes mixed tumors (sarco-carcinoma). (See also p. 316.)

THE STROMA OR FRAMEWORK OF CANCER

is the solid portion of the cancer remaining after separation of the cancer-juice (by pencilling, etc.), consisting of connective tissue, and not infrequently of the other remaining textures of the mother-organ.

The QUANTITY OF THE STROMA varies in a high degree. Only rarely is it so abundant, that it forms the by far greatest portion of the cancer, and, in microscopical examination, shows only few and small alveoli filled with cells: so-called SCIRRHUS, CARC. FIBROSUM. This is the case with many cancers during the whole of their existence, in the periphery of many cancers in so-called atrophic cancers. More often stroma and cancer-juice are present in almost equal proportions: COMMON CANCER, carc. fibroso-medullare. Most often, finally, the cells preponderate over the stroma in various degrees: MEDULLARY CANCER, CARC. MEDULLARE, cellular cancer. This may proceed to so great an extent, that the stroma forms only a very subordinate element of the cancer, or seems here and there to be entirely wanting (as in many medullary cancers of quick growth and in very old epithelial cancers): by subjecting it to water, by microscopical examination, etc., it becomes distinct.

The stroma of developed cancer consists sometimes of undulating connective tissue with scanty or abundant connective-tissue corpuscles; sometimes of non-undulating, indistinctly fibrous or entirely homogeneous connective tissue with for the most part scanty or less developed connective-tissue corpuscles, which, for certain distances, may be entirely wanting,— so that it resembles atrophic connective tissue. Rarely it consists only or chiefly of spindle or round cells, which are connected together like those of many sarcomata: CARC. SARCOMATOSUM. Very rarely it is more or less similar to mucous tissue: CARC. MYXOMATODES. In cancers, which are still in the process of development, the stroma consists of the more or less atrophic original tissue: thus in fatty tissue of connective tissue with atrophic fat-cells, in muscular tissue of atrophic muscular substance, in glands of gland-cells, etc. With the further development of the cancer the original tissues are often wholly destroyed. The stroma of bone-cancers, of many carcinomata situated on the surfaces of bones, rarely of those of soft parts, is either true bony substance in form of villous, laminated, etc., osteophytes, or a so-called osteoid substance.

Cancer with a mucous framework, CARCINOMA MYXOMATODES, is characterized by the stroma, which consists of mucous tissue; the textures immediately around the cell-accumulations show often a laminated structure, whilst the spindle-shaped cells are arranged in concentric circles. The cells of the alveoli are for the most part small, albuminous, and form rounded or oval masses in the alveoli; they are easily destroyed by fatty metamorphosis, so that sometimes the meshes are filled only with fatty detritus. The cells of the mucous tissue may be destroyed by fatty metamorphosis, so that in many cases in the framework as well as in the alveoli

only fat-granules are to be seen in place of the cellular elements.   Cancer with mucous framework is rare.   It is distinguished externally from common carcinoma only by its muco-gelatinous cut surface.

OSSIFICATION OF THE STROMA, the so-called OSTEOID CANCER,

occurs most often in cancers proceeding from the periosteum, as well as sometimes in secondary cancers, *e.g.*, of the lungs, rarely of other tissues. It affects for the most part connective-tissue cancers, rarely those of an epithelial formation.

THE BLOODVESSELS OF CANCER

course in the direction of the trabeculæ of the stroma.   They form a constant element in all these trabeculæ, with the exception of the thinnest, where they are entirely wanting.   In many very soft and vascular cancers the vessels are surrounded only by an extremely thin layer of soft connective tissue, which, in a superficial microscopical examination, is easily overlooked.   The vessels are capillaries of the usual diameter, and not infrequently are remarkably wide, and of the usual structure.   They are for the most part new-formed, but are connected in the usual manner with the arteries and venous branches of the surrounding structures.   In the lungs and liver the vessels of cancer are connected only with the nutritive vessels (bronchial and hepatic arteries), not with the functional vessels.   Larger arteries and veins are entirely absent in cancer, or are present only in its periphery and then are residues of the normal organ.   Only by their artificial injection is the number of the vessels of cancer demonstrated.

TELEANGIECTATIC CANCER, fungus hematodes, carcinoma teleangiectodes, is a very soft cancer, of a more or less dark red color, from the cut surface of which there flows an abundant, creamy juice of a red color, or a liquid similar to blood.   The not infrequent, slight grades of this form of cancer still show a varying number of points of the common character of a white cancer, which, in the highest degree, resemble capillary tumors, and which on section quickly become empty, so that only a dark red cavernous tissue without any or with only an indistinct cancerous structure remains.   The microscope shows, besides cancer-cells and blood-corpuscles, a for the most part delicate stroma with very abundant, and in high degree uniformly or partially dilated vessels.   This form of cancer occurs most often in the brain and kidneys.

LYMPHATIC VESSELS are probably of uniform occurrence in cancer.

SCHRÖDER VAN DER KOLK, already in 1842, demonstrated lymphatic vessels in cancer (*Dissert.* of LESPINASSE).   (See also p. 376.)

THE CAUSES OF PRIMARY CANCER

are in general the same as of other new-formations.   (See p. 367.)

On the causes of secondary cancer, that which has been said in general especially holds true (see p. 366).   Also here stand opposed the so-called implantation and infection theories.

It is most probable, that cells pass from primary cancers, through the lymph- or blood-vessels, into the circulation, and in the parts affected give rise to cancer-formation : so-called IMPLANTATION THEORY.   These points in many cases lie in the direction of the blood- and lymph-vessels ; in other cases secondary cancers arise in parts which stand in no immediate relation to the direction of the blood- and lymph-cur-

rent. They are of comparatively frequent occurrence in the large glands, as the liver and lungs.

Proofs of this manner of origin of secondary or metastatic cancers have in late years accumulated. For some cases it has been demonstrated with certainty, that cancer-masses as a whole and cancer-cells especially, which are free in the blood-vessels, having been transported hence and deposited in other parts, become the causes of cancerous formation. A case in point, of secondary cancer of the liver, has been communicated by SCHÜPPEL (*Arch. d. Heilk.*, 1868, IX., p. 387). See also FETZER, *Beitr. z. Histogenese des Leberkrebses*. *Täb. Dissert.*, 1868.

Proofs that cancers find their way into the LYMPHATIC VESSELS, are not infrequently found in autopsies: most often in primary or secondary cancers of the lungs, when the cancer is macroscopically visible in the interlobular subpleural lymphatic vessels. Cases of this kind have been observed by ANDRAL, HOURMANN, GÜNSBURG, CRUVEILHIER, ROKITANSKY, LEBERT, the author (*der Gebärmutterkrebs.*, p. 84. *Arch. d. Heilk.*, 1863, IV., p. 538), RECKLINGHAUSEN (*Mon. f. Gebrtsk.*, 1861, XVII., p. 322), but especially by KÖSTER (l. c.). Secondary cancerous degeneration of the LYMPH-GLANDS begins, according to LOEPER, most often in the surface, according to BILLROTH in the deeper alveoli; according to GUSSENBAUER (*Arch. f. klin. Chir.*, 1872, XIV., p. 561), it begins first in the gland-substance proper (glandular elements of the cortical and medullary sacs), and then in the tissue of the septa; degeneration in the medulla proceeds for the most part in the cortical portion.

Also in SEROUS MEMBRANES, secondary extension in a mechanical way is sometime to be demonstrated: particles of a soft cancer fall perhaps to the deeper parts of the cavity, here adhere and grow.

Opposed to the above theory is the INFECTION THEORY, whereby the juices arising from the primary cancer excite cancer-formation in those tissues with which they come in contact.

Experimental injection of cancer-juice into the bloodvessels of living animals has so far furnished no positive results. The experiments of LANGENBECK, of LEBERT and FOLLIN certainly have no value. O. WEBER (see p. 369) and GOUJON have perhaps obtained results; BILLROTH, LEBERT-WYSS, and DOUTRELEPONT, on the other hand, obtained negative results. REINCKE (*Virch. Arch.*, 1870, LI., p. 391) saw in two cases, where puncture of the abdomen had been performed on account of carcinomatous peritonitis, cancerous knots appear in the tract of puncture, which were separated from the peritoneal cancer by healthy tissue.

THE COURSE OF CANCER

is in the greater number of cases CHRONIC, lasting in so-called atrophic cancer and in many cases of epithelial cancer of external parts ten years, otherwise from one to about three years. The great variation in the course of cancer depends especially upon the kind and importance of the tissue attacked, upon the size and number, and upon the kind, of cancer (the rapidity of course is in general in direct ratio with the richness in cells and vascularity), upon their metamorphoses, surgical interference, etc.

Cancers of the mammary glands and of the uterus often run their course during pregnancy with remarkable rapidity (KLOTZ, *Ueber Mastitis carcinomatosa gravidarum et lactantium*. *Diss. Halle*, 1869).

Rarely the course of cancer is ACUTE, analogous to acute miliary tuberculosis: so-called ACUTE MILIARY CARCINOSIS. In such cases there is found for the most part an older cancer; much more rarely is the acute cancer primary. The symptoms are fever, which, in the former case, is associated with the symptoms of chronic cancer, often severe cerebral phenomena, symptoms on the part of the respiratory organs, etc., which in a few weeks lead to a fatal termination. Autopsy shows in various, sometimes in all tissues and organs of the body, especially in the serous membranes, sometimes even in new-formations, very numerous cancers, which are sometimes very small, sometimes of the size of a pea, isolated or confluent, grayish-

white, or grayish red; the serous membranes show besides for the most part symptoms of inflammation.

Köhler (l. c., p. 110), Rokitansky (*Lehrb.*, 1856, I., p. 255), Demme (*Schweiz. Monatsschr. f. pract. Med.*, 1856, No. 67), Bamberger (*Oestr. Ztschr. f. prakt. Heilk.*, 1857, No. 8 et 9), Erichsen (*Virch. Arch.*, XXI., p. 465).

The CHANGES presented by PARTS OF ORGANS FREE FROM CANCER either were present already before the new-formation, or are only consequences of the cancer. They cannot always be sharply separated. The most important of the changes dependent upon cancer are: hypertrophy, especially of the for the most part dilated muscular portions of saccular organs lying behind the cancer (intestinal canal from the œsophagus to the anus, uterus, urinary bladder), more rarely hypertrophy of glands, *e.g.*, sebaceous glands, also those of the normal papillæ or villi; atrophy, especially of glandular organs (liver, lymph-glands); catarrhs of the surrounding mucous membrane and their consequences: pigmentation, thickening, villous formation, ulcerations, hæmorrhages, false dropsies; more rarely croupous and so-called diphtheritic inflammations; pseudo-membranes and adhesions of the affected serous membrane; suppurative and septic inflammations of serous membranes, which are consequences of local cancer or of diseases consecutive to cancer (hydronephrosis, dilatations of the intestines, etc.), or stand in no demonstrable relation to cancer (pericarditis); venous thromboses (in consequence of pressure, cancer of the veins, marasmus). Often the parts free from cancer are perfectly normal (many cases of cancer of the stomach, cancer of glands, etc.).

The INFLUENCE OF CANCER ON THE WHOLE ORGANISM depends especially upon its size, number, its metamorphoses, but most upon its locality. Therefore most all cancers have at their beginning, some even until the death of the individual, no demonstrable general consequences. The latter, as well as final death, are dependent:

Most often upon the primary cancer: comparatively rarely upon the cancer which has not been at all or only little changed: its considerable size chiefly, seat in organs essential to life (brain), stricture or closure of canals essential to life (œsophagus, stomach); pressure on parts essential to life (brain, upper portion of the spinal cord), on many veins;

More often upon metamorphoses of the cancer: production of ichor and the consequent anæmia and cachexia (external parts, stomach, uterus); hæmorrhages, single and of large extent or frequent and less severe, especially from villous cancer (urinary bladder, stomach, uterus); perforations of surrounding parts, especially of large arteries, with fatal hæmorrhage (œsophagus), of the air-passages (cancer of the œsophagus), and serous membranes (consecutive inflammation, production of ichor);

More rarely upon numerous or quickly forming, for the most part small, miliary, secondary cancers (so-called acute carcinosis);

Upon a number of diseases, which clinically are of frequent occurrence in those sick with cancer, for which there is sometimes a manifest cause, thrombosis of veins, inflammations of contiguous serous membranes), sometimes none (pericarditis and endocarditis, pneumonia, especially in cancer of the œsophagus and stomach, dysentery, especially in uterine cancer, fatty metamorphosis of the heart, Bright's disease);

Upon affections, which are without connection with the cancer (*e.g.*, also pulmonary tuberculosis); as well as in ways wholly unknown.

The mortality from malignant tumors in Würzburg, from 1852 to 1855, reached 5.3 p. c. of the whole mortality. Of 100 cases of death from malignant tumors there were ; of the stomach.................................... 34.9 p. c.

uterus, vagina, etc............................ 18.5 "
large intestines and rectum.................... 8.1 "
liver, etc .... 7.5 "
face and lips.................................. 4.9 "
mammary glands................................ 4.3 "

Total........78.2 p. c.

A. EPITHELIAL CANCER, EPITHELIOMA.

(Cancroid in the broader sense.)

Epithelial cancer varies in gross and microscopic appearance, according as it is situated in the skin and in mucous membranes provided with pavement epithelium, or in mucous membranes provided with one or many layers of cylindrical epithelium, or in larger glandular organs. From this it receives the names : pavement-cell cancer, or cylindrical-cell cancer, or glandular-cell cancer. The two former have the form of a flat or deep, even tumorous infiltration, while the latter exists for the most part in form of knots.

Epithelial cancer arises always from forms of the external or internal germinal layer, thus only from the epithelium of the skin, mucous membrane, or glands. In the deepest epithelium, furthest removed from the surface of the skin or mucous membrane, there appears an increase of the latter, and a supplanting in similar manner of the non-epithelial tissues, as in the formation of the normal glands and of adenoma. The growing epithelial masses (epithelial rods, epithelial cylinders) are in size, form, etc., for the most part wholly irregular, atypical : they are for the most part large, of round, cylindrical or irregular form, and are frequently connected together in the form of a net-work ; they are for the most part without lumen ; the individual cells show no function (secretion). The basement membrane, at first present, later disappears. The epithelial masses grow into the surrounding parts with a larger or smaller base, and may finally be so far constricted as to become separate. The connective tissue in the surrounding textures is almost always permeated by abundant nuclei and small indifferent cells. A part of them is metamorphosed (as about foreign bodies, etc.) into connective tissue, and thus in part forms the cancer-stroma, others never reach this development, but finally decays with the epithelial cells. The largest portion of the stroma consists of pre-existing connective (or osseous) tissue, of atrophic gland-substance, etc. At the same time there is usually found in the tissue surrounding the epithelial masses a new-formation of blood- and probably also of lymph-vessels.

The GROWTH of epithelial cancer takes place, in large part, in the same manner as its first origin (peripheral growth), in small part by enlargement (nuclear increase, etc.) and increase of the already formed epithelial masses (central growth).

The view, that epithelial cancer and connective-tissue cancer are sharply distinct, and that epithelial cancer proceeds always from pre-existing epithelial, or gland-cells, has among its older advocates FÜHRER, who also first described the origin of epithelial cancer of the skin from the hair-follicles, and HANNOVER, FRERICHS, REMAK, in part also ROKITANSKY. But THIERSCH especially has further perfected

this theory and established it, especially with respect to epithelial cancer of the skin. It has been accepted by ROBIN, CORNIL, WYSS, NAUNYN, BILLROTH, WALDEYER, the author, W. MÜLLER and others. The supporters of the other view, that epithelial cancer arises commonly in the same manner as common cancer from connective tissue, are VIRCHOW, PAGET, FÖRSTER, O. WEBER, W. FOX, RECKLINGHAUSEN, CLASSEN, NEUMANN. The latter (*Virch. Arch.*, XXIV., p. 201) describes a cancerous development in the perineurium and neurilemma; POPPER (*Oestr. med. Jahrb.*, 1865, 4. II, p. 37) describes the same in transversely striated muscles. A third class assume an intermediate position. Thus, besides some of the last mentioned, RINDFLEISCH, who regards the epithelial outgrowths in the periphery of cancer as arising not from division or other increase of the epithelium at the diseased point, but by apposition from the sub-epithelial connective-tissue stratum. Also KLEBS, who assumes two kinds of epithelial cancer: simple epithelioma, which proceeds only from epithelial cells, and the so-called infectious epithelioma, which arises from a metamorphosis of other elements into epithelia (*Virch. Arch.*, XXXVIII., p. 214). See further R. MAIER (*Lehrb. d. allg. path. Anat.*, 1871, p. 417), LEONTOWITSCH (*Med. Ctrlbl.*, 1869, No. 13), VOLKMANN (*Virch. Arch.*, 1871, L., p. 543).

THIERSCH and his followers adduce the following reasons for the epithelial origin of epithelial cancer: the mode of development, especially the development of epithelium of the skin and mucous membranes and their derivatives (the epithelium of serous membranes, etc., and that of the urino-genital system have. as is known, another origin: see p. 395)—but epithelial cancer occurs primarily in only the first mentioned; losses of substance, which are constantly suffered by epithelium, are repaired by the epithelium itself, not by the connective-tissue corpuscles of the vascular stroma (see p. 463); also with respect to pathological cases has the epithelium-forming capacity of the stroma not yet been shown (see p. 470); the connection between the epithelium of epithelial cancer and that of the affected skin or mucous membrane can, on the boundaries of the former, not infrequently be directly demonstrated. The statement, that epithelial cancer appears as a primary degeneration removed from epithelial forms of the skin and mucous membrane (in bones, lymph-glands, etc.), does not exclude the former possibility, *e.g.*, its origin from the sweat-glands. Also in the origin of dermoid cysts, of cholesteatoma, as already stated by REMAK, as well as of epithelial cancer, it may happen, that epithelial germs of the horny layer, as well as of intestinal glandular layer, reach by a pathological process into the deep structures, in which they lose every connection with the epithelial matrix by constriction; here, like the enamel-germ destined for the permanent tooth, they may remain latent for years, without losing their capacity for development. (See with respect to like peculiarities of the middle germinal layer: enchondroma, myxoma.) THIERSCH's view on epithelial cancer has, in the more recent results of epithelial regeneration, received a further, although only an indirect support. Many cases of cancer, which cannot be explained by THIERSCH's theory, are endothelial in character.

The opponents of THIERSCH's theory hold that the most different tissues are not alone produced by the cells of the ovum, but that this capacity is enjoyed by all or indeed by most young cells, especially granulation-cells arising from connective tissue and the colorless blood-corpuscles. (Consult O. WEBER, *Virch. Arch.*, XXXIX., p. 254.) Or they seek the demonstration of an epithelial or epitheliomal formation in parts or organs which contain no epithelium derived from the upper or lower germinal layer: thus VIRCHOW (*Arch.*, VIII., p. 414) with respect to cholesteatoma, EBERTH (*Ib.*, XLIX., p. 51) for a similar new-formation, ARNDT (*Ib.*, LI., p. 495).

According to RECKLINGHAUSEN (*Würzb. med. Ztschr.*, VII., p. 24) and KÖSTER, the well-known processes of cancroid are cell-formed casts of the lymphatics. This is supported by the extensive distribution of the lymphatic vessels and glands, as well as by the so frequent formation, at points of the youngest development, of complete net-works, which are entirely conformable with the pre-existing net-work of lymphatic vessels. WALDEYER found similar conditions in intestinal cancers, and not in other cancers.

The VARIETIES OF EPITHELIAL CANCER are:

a. PAVEMENT-CELL CANCER (or epithelial cancer, EPITHELIOMA or CANCROID in the narrower sense).

PAVEMENT-CELL CANCER forms more rarely a more or less sharply

defined knot, but commonly assumes the form of a diffuse, in parts tumorous infiltration. It is usually of little extent, shows an uniform or knotted thickening, and by long duration there is often formed in the centre a crater-like ulcer, which secretes a small quantity of pus and white atheromatous-like mass which then easily dries on the external parts. Or the cancer forms a more varying ulcer, which reaches one square inch in size, and is grayish-white, grayish-red, rarely dark-red, for the most part presenting large granulations, and is often covered with crusts, and with moderately thickened flat or knotty, smooth or warty borders. The cut-surface is usually white or grayish white, for the most part moist, more rarely dry and crumbling, smooth or finally granular, rarely homogeneous or fibrous, or fleshy or glandular; it is rarely distinctly juicy. Except in the very rare cases of encapsulation (see also Cholesteatoma), the periphery shows either a gradual transition into the normal tissues, or it contains apparently sharply defined, process-like masses. By scraping or squeezing there escape from the chief mass, besides a for the most part scanty, serous or rarely creamy liquid, bodies like comedones, which are whitish and of varying size. The centre contains sometimes one or more, for the most part sharply defined cavities with dry, grayish white, atheromatous contents.

The pavement-cell cancer occurs as a PRIMARY FORMATION most often on the skin, especially on those portions of it which are transitions into mucous membrane (lower lip, around the external opening of the nares, the eyelids, the ear, the anus, the external male and female genitals) and in mucous membranes with laminated pavement epithelium (especially on the tongue, in the œsophagus, on the affected parts of the larynx, in the vagina and vaginal portion of the uterus), more rarely in the pharynx, conjunctiva, and bones. From the first mentioned parts the cancer progresses into the deeper layers of the skin and mucous membranes, on the latter through the submucous tissue, through the intermuscular tissue to the surface of the affected membrane, farther on into the neighboring organs (in the œsophagus, e.g., into the mediastinum, into the trachea, lungs, etc., in the vagina to the urinary bladder and rectum), even into the bones. Epithelial cancer is found as a SECONDARY formation after some duration often in the appertaining lymph-glands, more rarely in the veins, in internal organs, especially the lungs and liver.

Epithelial cancer arises either PRIMARILY, or IN OTHER NEW-FORMATIONS, most often in cicatrices and warts, probably also through metamorphosis of adenoma of the sebaceous, or sweat-glands of the skin, of the mucous glands of the affected mucous membranes. CZERNY (*Arch. f. klin. Chir.*, 1869. X., p. 894) describes an epithelial carcinoma, which was developed from a congenital sacral tumor. This cancer is of remarkably frequent occurrence, especially that of the skin, in men from 40 to 50 years old and more, and in those of low condition. It has not yet been observed before the 30th year.

Cure not infrequently results in external cancer, after extirpation which has been performed at the right time and entirely.

HISTOLOGICALLY, the pavement-cell cancer differs. Either the peripheral cancer-cells are small, cylindrical, sometimes lightly pigmented, perpendicular to the stroma, distinctly nuclear; the succeeding cells are large or very large, cubical or flat, quadratic, rhombic, rectangular, club-shaped, etc., usually with spines, with for the most part distinct, of medium size or large, usually a single, more rarely multiple nucleus and distinct nucleolus, rarely without nucleus; the most internal cells are often concentrically

laminated about a clear, homogeneous or nucleated centre, flattened in
the highest degree, fibre-like, without nucleus : so-called nests, horny
bodies, pearl-globules, *globes épidermiques.* Or, the cells are flat, of vary-
ing form, for the most part rhombic or elongated, for the most part with
a large distinct nucleus. Rarely the cell-masses are surrounded by a homo-
geneous membrane. The alveoli of both forms are of very varying size,
sometimes macroscopical ; their form is sometimes regularly round or oval,
sometimes irregularly pouched, glandular, forked or arborescent. The vas-
cular stroma is for the most part scanty, and occupied here and there by
abundant free nuclei and small round cells. Sometimes these are to be dis-
tinguished with difficulty from those of the alveoli. In some cases, which
have an appearance similar to chronic common or lupous ulcers of the skin,
the stroma is very vascular and cellular like granulation-tissue, and the
epithelial masses, on the other hand, appear very far in the background.

THIERSCH distinguishes a SUPERFICIAL and a DEEPLY ATTACHED epithelial cancer
of the skin. The former shows an epithelial new-formation, superficial in extent,
of few mm. in thickness, which on perpendicular section is sharply separated from
the stroma ; the latter, on the other hand, extends without such sharp limitation to a
considerable depth in form of irregular masses. The superficial epithelial cancer is
found for the most part only as a superficial ulcer with superficial or slightly thickened
borders. and presenting no anomalies of the immediately surrounding textures ; the
deep cancer as a rule forms ulcers of very irregular form, and there are always found
hard conglobate knots of the size of a pea to that of a walnut, partly in the surround-
ing, partly in the underlying structures. Both advance destructively from the surface
into the subjacent textures, whilst at the same time their circumference becomes
larger : the superficial more slowly than the deep cancer. Both, especially the deep,
may or may not be connected with papillary, vascular growth of the stroma (warts or
villi). According to WALDEYER, the superficial epithelial cancer as well as the *ulcus
rodens* of the skin, proceed especially from the deeper layers of the stratum Malpighi,
extend however only a little in depth, before they become ulcerous. The deep cuta-
neous cancer, on the other hand, the variously large knots of which are apparently
developed primarily deep in the cutis or in the subcutaneous tissue, always proceeds
from the sebaceous glands, and later also from the interpapillary layer of the rete
Malpighi, rarely also from the sweat-glands and from the sheaths of the roots of the
hair. (See Glandular cancer.)
    The cells of pavement epithelial cancer of the skin and mucous membranes are
not smooth, but show distinct, radiating lines, which, according to M. SCHULTZE
and others, are delicate spines, by which the cells adhere to one another. but which,
according to SCHRÖN, are tubular pores,—as occurs similarly on the cells of the
rete Malpighi, etc. (M. SCHULTZE, *Virch. Arch.*, XXX., p. 260.—SCHRÖN, *Moleschott's
Unters.*, IX.).
    BIESIADECKI (*Wien acad. Ber.*, II., LVI.) uniformly found wandering cells
between the epithelial cells of the normal skin. WALDEYER observed these in almost
all preparations of carcinoma of the most diverse organs. They never appear to pass
into epithelial, or cancer-cells.
    BIZZOZERO (*Oestr. med. Jahrb.*, 1873, p. 121) found in a case of pavement epithe-
lial cancer of the cheeks, between the epithelial processes and stroma, vessel-like
spaces lined with endothelium. which spaces could be injected from the bloodvessels,
and which in the large alveoli formed a net-work.
    The small round cells in the stroma of cancer arise, according to most, through
division of connective-tissue corpuscles, according to others (BILLROTH), they are
migrated white blood-corpuscles. As carcinoma granulosum superficiale, WALDEYER
designates those superficial cutaneous cancers, the abundant stroma of which,
through very dense small-cell infiltration, is similar to granulation-tumor, especially
lupus, while the epithelial growth retrogrades.

VARIETIES OF PAVEMENT-CELL CANCER.

The PAPILLARY or WARTY PAVEMENT-CELL CANCER is characterized by the
nature of its surface, which is similar to that of warts or pointed condy-
lomata; in ulcerating cancers to that of the base of the ulcer. It is pale

or red, in proportion to the number and size of the vessels. It occurs most often on the glans penis and prepuce, on the clitoris, on the vaginal portion of the uterus, in less degrees of papillary formation not infrequently also on the lower lip. Histologically, it shows numerous, simple or branched connective-tissue tufts, which proceed from the common stroma, and which are surrounded by abundant or scanty flat cells. If ulceration has appeared, there will not infrequently be seen on the base and in the borders of the ulcer papillæ with numerous broad vessels, and sometimes strong small cell infiltration, which reaches as far as the epithelium.

Sometimes the same villous formation is found also in the interior of the alveoli. Then there appears the DESTROYING PAPILLARY TUMOR, formerly so-called.

Between papillary epithelioma and papillary fibroma (see p. 394) there are probably transitions.

β. CICATRICIAL PAVEMENT-CELL CANCER

occurs, for the most part in the skin of the face of old people, as a superficial, slowly growing cancer, in which there appears a gradual retrogression and resorption of the largest portion of the cells and a cicatricial contraction of the stroma. Thus there arise in the periphery superficial, infiltrated cicatrices without previous ulceration.

γ. MUCOUS CANCROID, GELATINOUS EPITHELIAL CANCER, CYLINDROMA (sacculated sarcoma, etc.), occurs, either in combination with common or papillary pavement-cell cancer, or appears from the beginning as a peculiar variety of the former. It is especially characterized by the formation of numerous cylindrical, club-shaped or arborescent masses, which consist of mucous substance or mucous tissue, and which, if present in large masses, give the tumor a mucous or gelatinous appearance. Mucous cancroid is found chiefly in the bones of the face, especially the superior maxilla, and in the skin of the face, rarely in serous membranes.

The hyaloid formations of mucous cancroid or cylindroma have been differently interpreted by different observers. Many regard them as cells of the nature of connective tissue or cartilage, which suffer mucous degeneration, greatly enlarge, receive processes, etc.; others regards them as the strongly swollen adventitia of the bloodvessels, which had suffered mucous degeneration; yet others regard them as increased and changed endothelium of the lymphatic vessels. The mucous substance may later be metamorphosed into fibrous tissue; growths may arise from the cells; the vessels may by obliteration be transformed into solid cylinders; etc.

Most probably many cases of cylindroma do not belong to cancer, but to other new-formations, the cells of which, by a peculiar distribution, become mucous, or their stroma in like manner degenerates into mucous tissue. (See p. 481.)

HENLE, *Ztschr. f. rat. Med.*, III., p. 131.—BUSCH, *Chirurg. Beob.*, 1854, p. 296. —BILLROTH, *Unters. üb. d. Entw. d. Blutgefässe*, 1856; *Virch. Arch.*, XVII., p. 357; *Arch. d. Heilk.*, III., p. 47.—ROBIN, in Lebert's *Tr. d'anat. path.*, Atl., T. XLIX. et XL.—MECKEL, *Chir.-Ann.*, VII., pp. 89 et 103.—VOLKMANN, *Virch. Arch.*, XII., p. 293.—MAIER, *Ib.*, XIV., p. 270; *Arch. d. Heilk.*, VII., p. 145.—O. WEBER, *Chir. Erf.*, p. 371.—FRIEDREICH, *Virch. Arch.*, XXVII., p. 375.—RECKLINGHAUSEN, *Arch. f. Ophthalmol.*, X., p. 190.—BÖTTCHER, *Virch. Arch.*, XXXVIII., p. 400.—KÖSTER, *Ib.*, XL., p. 468.—FÖRSTER, *Hdb. d. path. Anat.*, 2, *Aufl.*, I., p. 441.—PAGENSTECHER, *Virch. Arch.*, XLV., p. 490.—BIRCH-HIRSCHFELD, *Arch. d. Heilk.*, 1871, XII., p. 167.

CARCINOMA ADENOIDES is a term applied by WALDEYER to that form of

cancer, the alveoli of which are distinguished by a glandular sac-like form, while the stroma is only lightly infiltrated with small cells,—also with the cancer proceeding from glands.

Metamorphoses of pavement-epithelium cancer.

Cornification of the central or of all the cells of the alveoli : the former occurs so often, that the resulting forms were formerly regarded as characteristic of epithelial cancer ; the latter forms the condition of cholesteatoma (*vide infra*).

By complete simple atrophy, as it were drying of the cells of pavement-cell cancer, especially of those limited by a capsule, there arises the so-called horny shell-epithelial cancer (Förster), carcinoma keratoides s. corneum (Waldeyer). These cancers are harder and dry ; the cut surface shows white, dry, brittle, homogeneous or partly laminated masses of varying size and form.

Dry cancroid (Förster, *Würzb. Verh.*, X., p. 162) consists in this, that the cells, shortly after their formation, become dry and partly contain air ; hence the tumor is distinguished by its unusual dryness and lightness. The air-containing cells lie in the middle portion of the alveolus ; the peripheral cells contain no air.

Fatty metamorphosis of the cells is always present in lighter degrees in old cancers ; its higher degrees lead to softening of the cancer, which is followed in its superficial parts by ulceration, in the deeper and central portions by atheromatous softening and cavities, even cysts. (*Vide infra.*)

Mucous softening occurs rarely and for the most part only in its lighter grades.

Cancroids with total calcification and ossification, so that they resemble stony circumscribed concretions, have been described by Förster (*Würzb. Verh.*, X., p. 162) and Sokolowsky (*Z. f. rat. Med.*, 1864, XXIII., p. 23). In one case the cells and stroma were calcified, and no vessels were demonstrable ; in another, the latter were still present and permeable.

b. Cylinder-cell cancer (cylinder-epithelial cancroid).

The cylinder-cell cancer has commonly the form of a more or less sharply defined, but never encapsuled infiltration, which at first occupies only the mucous membrane and submucous tissue, later also the muscular, serous and surrounding tissues of the affected hollow organ. The infiltration is of varying extent and thickness, in hollow organs (stomach, intestine, uterus) often affecting the whole periphery (so-called annular cancers). At a later period the middle portion often becomes ulcerous, especially in the stomach and intestines. On section the peripheral parts, as well as the centre, so far as it is not ulcerated, show, in place of the various tissue-layers (in the muscular tissue at first only the intermuscular connective tissue, but later the muscle proper), a white, gray, or reddish, rarely hard, usually in various degrees soft, for the most part perfectly homogeneous, rarely at points, fibrous substance. By scraping, the cut surfaces, sometimes throughout and uniformly, sometimes only from numberless very small openings, commonly gives off an abundant, weakly mucous or distinctly creamy liquid, of the same color as the cut surface. In many cases the cut surface shows a very delicate or grosser net-work, in the very small (or of the size of a millet seed and larger) spaces of which there is contained a distinctly creamy or slightly cheesy juice, which in the former case uniformly covers the cut surface, in the latter it is evacuated in the form of maggots ; after evacuation of the juice the spaces appear as smooth pits

(*cancer aréolaire pultacé*), or they contain a macroscopical, very delicate, or microscopical cellular framework.

Cylinder-cell cancer occurs PRIMARILY only on mucous membranes with a uni- or multi-laminated cylindrical epithelium, especially on narrow portions of these, or in places where one section of mucous membrane passes into another, most often on the vaginal portion of the uterus, where it for the most part occupies almost equal portions of the uterus and vagina, in the pylorus of the stomach, where it rarely and usually only at points passes over on to the duodenum, in the large intestine; more rarely is it in the cardiac and other portions of the stomach, in the cæcum, in the flexures of the colon, in the air-passages, urinary bladder, etc. Also there belong here many cases of cancer of the mammæ and liver, in which the cancer proceeds from the milk-, or bile-ducts. Cylinder-cell cancer occurs, TRANSPLANTED, in the appertaining submucous tissue, when it reaches its greatest extent, in the (normal or hypertrophic) muscular and serous tunics, not infrequently in all the adjacent organs (in uterine cancer the urinary bladder, rectum, etc., in pyloric cancer the peritoneum, the boundary connective tissue of the hilus of the liver, the liver itself). SECONDARILY, it is often found in the connected lymph-glands; if it occurs within the radicles of the vena portæ, especially often in the liver; in both cases also not infrequently in the lungs, in some serous membranes; rarely in other organs.

Cylinder-cell cancer occurs also sometimes in previously normal, sometimes in OTHERWISE DISEASED mucous membranes: in the stomach I have often seen cases, where it had developed in the vicinity of old cicatrices of ulcers. (Consult also W. MÜLLER and WALDEYER.) In the uterus it is not infrequently found in existing so-called chronic infarction of it. A transition of adenoma of mucous membranes into cancer is likewise probable.

MICROSCOPICALLY, cylinder-cell cancer shows cells of more or less distinct cylindrical form. Their arrangement corresponds to the normal arrangement of cylindrical epithelium. The cells are rarely wholly like those of the affected mucous membrane; for the most part they, as well as their nuclei, are larger and less regularly cylindrical, even spindle-shaped, caudate, etc. Or only the cancer cells which lie in the periphery of the alveoli are distinctly cylindrical; those lying further inward have an irregular, often quadratic, caudate, even stellate, etc., form; those in the centre are for the most part rounded. The cancer-cells are arranged almost at right angles to the stroma (the membrana propria is for the most part wanting), rarely at an acute angle, sometimes indeed almost parallel with it: in the latter case cancer-tissue may bear a similarity to the tissue of sarcoma. The stroma is for the most part less thick, and usually very vascular. The alveoli are of medium size or large, oval, cylindrical, irregularly distended, gland-like, etc. Their form is, besides in brushed sections, even with the cells, easily to be recognized, whilst the latter often are so adherent that they may be removed from out of the alveoli *en masse*.

Here belongs also that form, occurring especially in the mamma and lymph-glands, where in the examination of the fresh preparation there occur no common cells, but large masses, similar to mother-cells with daughter-nuclei, representing perfect casts of the alveoli, hence cylindrical, club-shaped, etc., which masses are sharply defined, and consist of a homogeneous, finely granular basis substance, and for the most part large, round or oval nuclei, with large nucleoli, which lie quite near one another and quite regularly arranged: so-called hollow clubs, germ cylinders, *tissu hétéroadénique.* After a longer time, or subjection to the action of a solution of chromic acid, chromate of potash, etc., the individual cells for the most part appear.

The TERMINATION of cylinder-cell cancer of the mucous membranes is determined by the cylinder-cells of the mucous membranes themselves, but especially by the epithelium of the affected glands of the mucous membranes: in the stomach the peptic and mucous glands, in the intestines the glands of Lieberkuhn, in the uterus the sacculated glands. A group of them pushes into the deep portions of the mucosa a number of shoots, which in the submucous tissue grow with especial vigor and form infiltrates or knots, which may only at a small point be connected with the glands, from which they proceeded. Accordingly, most cases of cylinder-cell cancer should be included among the glandular-cell cancers. But a sharp limit between the epithelium of the mucous membrane and that of the upper portion of the glands is already physiologically in most places not to be drawn.

VARIETIES OF CYLINDER-CELL CANCER.

VILLOUS CANCER, CARCINOMA VILLOSUM, is a combination of a for the most part soft villous tumor with cylinder-cell cancer. It occurs in its pure form only on mucous membranes (urinary bladder; uterus and vagina: so-called cauliflower growth of the vaginal portion of the uterus; stomach, etc.), rarely in parenchymata. In the former localities it forms masses of a size which varies to that of the fist and larger, which are more or less sharply circumscribed, grayish or dark red, rarely pale, which masses are soft and rich in juice and furnish an uniform or (especially by examination under water) distinctly villous structure. Soft large villous cancers of this kind are for the most part sharply circumscribed, and are seated on the mother-tissue by a broad or small pedicle, which in the latter case is short or long; more rarely they are diffuse, high in the middle, gradually disappearing toward the periphery. The base of villous cancer shows a distinct infiltration with cylinder-cell cancer. On villous cancer in parenchymata, *vide infra*.

MICROSCOPICAL investigation of villous cancers offers in general the characters of soft villous tumors (see p. 394). Their stroma consists of simple or branched, delicate or thicker connective-tissue masses, which in the centre contain for the most part numerous and wide vessels, and at their base pass immediately into cancer-stroma. The villi are surrounded by a single or multiple layer of cylindrical cells. Either the cells surround only the single villi, or around all the villi there is found besides a common manifold deposit of cells: in the former case the tumor has a distinctly villous character; in the other, the latter appears only after artificial separation of the common cell-covering.

The slightest, only microscopically visible degrees of villous cancer not infrequently occur on mucous membranes of every kind, also without papillæ, above the cancerous infiltration of the mucous membrane or in the textures surrounding it.

The remaining varieties of cylinder-cell cancer are the same as those of pavement-cell cancer.

THE METAMORPHOSES OF CYLINDER-CELL CANCER

are chiefly fatty and mucous metamorphosis: the former in its higher grades leads to softening with formation of cavities or with ulceration, the latter to so-called colloid cancer. (*Vide infra*.)

c. GLANDULAR CELL CANCER, GLANDULAR CARCINOMA.

The glandular cell cancer, hitherto sometimes ranked with soft connective

cancer, sometimes with cylinder-cell cancer, is not yet so well known that a general description of it can be given. It exists always in the form of one or more, even very numerous apparently sharply-defined knots of varied size, which in all essential, gross anatomical and histological relations resemble INFILTRATION OF CYLINDER-CELL CANCER. Not infrequently the cancer-cells are small and less distinctly epithelial. If the quantity of cells is very great and that of the stroma scanty, the separation of this form from soft connective-tissue cancer will be possible only by careful examination. If the stroma is very abundant and the alveoli few and small, there will arise the hard glandular carcinoma, the so-called scirrhus. Sometimes the stroma, like sarcoma, is composed of spindle cells. This has most often been observed in the kidneys and testicles, giving rise to very large tumors. In many cases the stroma is very vascular: teleangiectatic form.

The glandular cell cancer is the most frequent PRIMARY form of cancer of the large true glandular organs, especially the mammæ, also the liver, salivary glands, prostate, kidneys, ovaries and testicles, in part also the skin (sebaceous and sweat-glands) and mucous membranes (gastric, intestinal, mucous glands). It is found TRANSFERRED and SECONDARY in like manner as cylinder-cell cancer, the latter most often in lymph-glands, lungs, and liver.

LANGHANS (*Virch. Arch.*, 1871, LIII., p. 470) describes a primary cancer of the trachea and bronchi; KNOLL (*Ib.*, 1872, LIV., p. 378) one of the larynx, which probably proceeded from the mucous glands.

Glandular cell cancer takes its starting-point in the racemose glands of the smallest gland-ducts and terminal vesicles of the glands,—from those in the sacculated glands of the mucous membranes, the kidneys, testicles, etc., from the closed follicles in the ovaries and thyroid gland. In many cases it passes into cylinder-cell cancer. In other cases it arises in the same manner as ADENOMA (see p. 472): but while in this the new-formed cells resemble in size, arrangement, etc., those of the affected normal glands, here the new-formed cells grow in greater number, with less regularity, etc., into the bordering tissues.

Doubtless, between adenoma and glandular cell cancer, there are found the most manifold TRANSITIONS (adenoma carcinomatodes), most often in the mamma and ovary. These affect the tumor as a whole, as well as the individual parts of it; the first beginnings of adenoma, as well as after a longer existence; pure adenoma, as well as its metamorphoses (kystoma, etc.).

GRIESINGER and RINDFLEISCH (*Arch. d. Heilk.*, V., pp. 385 et 395) describe as ADENOID OF THE LIVER a new-formation, which had the form of sharply circumscribed, of varying size, and variously colored, soft knots of liver-tissue, and which occurred in very large number, and was followed by destruction of the largest portion of the liver with icterus, œdema, marasmus, and death. This must now be included here.

With respect to the liver, it is more often doubtful whether the so-called epithelial cancer arises from the epithelium of the bile-ducts or from the liver-cells (NAUNYN, l. c., p. 717). In the mamma, WALDEYER distinguishes the primary cancer of the terminal gland-vesicles (so-called parenchymatous cancer), and the cancer which proceeds from the larger milk-ducts (so-called galactophores).

NAUNYN (*Arch. f. Anat., Phys. u. wiss. Med.*, 1866, p. 710) describes a cystosarcoma of the liver, analogous to that of the mamma (REINHARDT, MECKEL, and others), which proceeds from the bile-ducts through dilatation of them in consequence of an increase of their epithelium and through increase of the connective tissue sur-

rounding them, and further on with participation of the proper liver-cell spaces. The tumors were numerous, and reached the size of a millet seed.

On cancer of the testicle, consult HIRSCHFELD, *Arch. d. Heilk.*, IX., p. 537.

According to RINDFLEISCH (*Lehrb.*, 1873, p. 142), hard glandular carcinoma depends upon an interstitial inflammation of slow progress, the cellular products of which are metamorphosed into epithelial forms instead of into pus or connective tissue—in consequence of an "epithelial infection" (KLEBS): *i.e.*, some young epithelial cells penetrate into the intervening spaces of the neighboring connective tissue and infect the indifferent cells found here.

WALDEYER proposes to call the cancer found in glandular organs tubular or alveolar cancer, according as it proceeds from the excretory ducts or from the alveoli.

The METAMORPHOSES OF GLANDULAR-CELL CANCER are the same as those of cylinder-cell cancer.

METAMORPHOSES COMMON to the three forms of epithelial cancer.

Most epithelial cancers show, after a longer or shorter existence, a series of metamorphoses, which are sometimes unessential and are recognizable only microscopically, sometimes completely change the appearance of the cancer here and there or throughout. Many of these metamorphoses are also of great clinical interest.

The changes affect either the cancer-cells, or the stroma, in higher degrees for the most part both at the same time.

FATTY METAMORPHOSIS AND SIMPLE ATROPHY are the most frequent changes of cancer-cells. They occur for the most part together. Macroscopically, the change varies according to the degree and the preponderance of one or the other. The lower degrees, occurring in almost every·cancer, are not recognizable by the naked eye. The higher degrees are likewise not infre-quent; they are usually most marked at the centre of the cancer; rarely they affect almost the whole mass. Through both metamorphoses sections of the cancer receives a grayish-yellow or yellowish color, which is rarely uniform, for the most part presenting a regular or irregular, fine or large net-work, or is punctated: so-called CARCINOMA RETICULATUM. The portions affected are also dry, juiceless, smooth (like yellow tubercle: so-called TUBERCULIZATION of cancer), and bloodless. The centre of these knots is remarkably hard, if there has been an abundant resorption of the degenerated cells. At other times, if the stroma is scanty, etc., the centre softens or even forms a cavity (CAVERNOUS CANCER). If fatty metamorphosis preponderates strongly over simple atrophy of the cancer-cells, the cancer thereby becomes softer, greasy, like butter or pus.

Not all yellow dry parts of the cancer section depend upon the changes mentioned. They are not infrequently only changed portions of the normal tissue: *e.g.*, in the gland-ducts of the mamma filled with colostrum, in the lungs and bronchi with thickened secretion, or in thrombosed vessels.

The causes of the above metamorphoses are most often atrophy of the cancerous vessels, sometimes numerous small hæmorrhages. According to WEDL (*Wien. Sitzungsber.*, 1859, XXXVII., p. 265), the so-called carcinoma reticulatum is dependent upon the bloodvessels which have suffered cancerous metamorphosis and are infiltrated with fat.

Both metamorphoses are followed by destruction of the cancer-cells and their resorption, and in their higher degrees they are the conditions of the umbilicated state or atrophy of the cancer.

The umbilical formation of cancer-knots consists in the formation of one or a few deep peripheral pits, which occurs especially in cancers of the mamma and liver, more rarely in those of the lungs, stomach and intes-

tines. In the mamma there sometimes arises at the same time a cicatricial retraction of the larger milk-ducts, and hence traction upon the nipples, and a sinking in of the latter. The skin is firmly attached to these cancers, otherwise normal; the serosa is rarely normal, for the most part thickened, rich or poor in vessels. On their cut surface the umbilicated knots always show a higher degree of fatty metamorphosis and simple atrophy of the cancer-cells; in the centre also there is often an abundant fibrous substance, i.e. cancer-tissue, the cells of which, after the above metamorphoses, are for the most part or wholly resorbed, while the stroma remains.

The so-called ATROPHIC CARCINOMA, according to many, the so-called SCIRRHUS, arises if the cancer is not too rich in cells and the alveoli small, if fatty metamorphosis and simple atrophy gradually affect all the cancer-knots, and if there follows a resorption of the fatty and simple detritus. The affected, organ is then not enlarged, but has generally, or at the point affected a smaller volume, is here often depressed, firmly attached to the subjacent skin, and feels like a hard cicatrix. The sinking in is sometimes so much the more marked, if there occurs in the surrounding structures an hypertrophy of other tissues, e.g., of the fat-tissue. On section, there is seen sometimes only cicatricial tissue, sometimes, besides, a pale, lardaceous hard substance (so-called *cancer lardacé*), rarely, most often in the periphery, a softer cancer-tissue, which is unchanged or undergoes fatty and simple atrophy. The appertaining lymph-glands are sometimes likewise atrophic, sometimes distinctly carcinomatous.

These changes occur most often in older people, in cancers especially of the female mamma and of the stomach, more rarely of the lymph-glands, pleuræ, in epithelial cancers (see p. 489). Their course is for the most part very chronic, lasting from 10 to 20 years.

Of many cases especially of the stomach and mamma, even after careful microscopic examination, it remains doubtful whether they belong here, or whether they represent chronic inflammations with strong cicatricial formation or with simultaneous glandular hypertrophy.

MUCOUS METAMORPHOSIS of cancer-cells is the condition of a varied appearance of the cancer, according to its extent, its degree, and the consecutive changes of the stroma and vessels. It is most frequent in cylinder-cell cancer. Here it is observed in two different degrees.

A SLIGHT EXTENT OF MUCOUS METAMORPHOSIS, and its diffusion over all or most of the parts of the cancer, is quite frequent and is the condition of the mucous character of the cancer-juice. Its quantity varies: sometimes it is so small, that the known creamy character of the juice is little affected; sometimes so great that the mucous character immediately becomes distinctly marked. The latter sometimes extends uniformly over the whole cut surface, sometimes it is found only in isolated parts of it.

HIGH DEGREES OF MUCOUS METAMORPHOSIS are the condition of the so-called COMBINATION OF COMMON AND GELATINOUS CANCER.

In the lower stages of this degree, isolated and sharply circumscribed portions of the cut surface are found remarkably pale, and soft; from them there flows a thin or thick mucous liquid, as clear as water or filled with fine yellow points. The remaining portions of the cancer behave in a normal manner, or show here and there simple atrophy or fatty metamorphosis.

In the higher stages there are commonly observed in various portions of

the cancer and quite irregularly distributed, very small, to the size of a pea, or bean and larger, rounded or irregular, grayish white, greenish, or yellow punctated spots, which are somewhat prominent over the cut surface. They correspond to cavities, which are filled with mucous masses. In most cases the superficial extent of these mucous cavities is small. Sometimes, however, the mucous cavities so greatly exceed in extent the unchanged portions of the cancer, that the latter may easily be overlooked. The former then are not infrequently of the size of a walnut and larger. Their form is rarely round, for the most part irregular. The mucus contained in them, after section, wells up over the surrounding structures, and is for the most part very tenacious. Mucous metamorphosis occurs in these high degrees sometimes only in primary cancer, especially in those of the stomach, sometimes also in some or all secondary cancers. It rarely occurs in the latter alone.

Mucous metamorphosis of cancer-cells shows MICROSCOPICALLY no essential distinction from the mucous metamorphosis of physiological cells. (See p. 332.) In its higher grades there results atrophy of the cancer-stroma, and especially of the vessels.

The stroma of the degenerated portions is liable to changes, which in themselves have no peculiarity, but which, on account of their similarity with gelatinous cancer, deserve an especial consideration. They are only the consequences of the considerable increase of the contents of the alveoli through mucous metamorphosis of their cells. The alveoli are commonly oval or round, almost never present distentions, or otherwise irregular forms ; they are for the most part very large. The stroma itself, in the degenerated parts, is very slight ; its fibres are no longer wavy, but stiff, and therein is still distinctly fibrous, or it presents fibre-like folds or is entirely homogeneous. Its corpuscles are in all cases very small and undeveloped ; very often there is observed in their place spindle-shaped or filamentous accumulation of fat-drops, or they appear to be entirely absent. Vessels occur within the stroma very rarely. Finally, in the middle of many large mucous spaces, the stroma is entirely absent : there is observed in the peripheral portions the already described relations of the trabeculæ of the stroma ; toward the middle, the latter become gradually smaller, and terminate for the most part in free and fine-pointed extremities.

GELATINOUS CANCER, COLLOID CANCER, ALVEOLAR CANCER (mucous cell cancer) is that form of cancer, in which, in place of the common cancer-juice, there occurs a grayish white, clear or slightly clouded, mucous or gelatinous, liquid or tenacious substance (hence the names gelatinous and colloid cancer, gum-cancer), and where the stroma offers for the most part an exquisite alveolar structure, visible to the naked eye (hence the name alveolar cancer). The further peculiarities of this cancer are : its occurrence confined for the most part to certain organs (stomach, large intestine, peritoneum,—uterus, mammary glands), its usual appearance in form of an infiltration, its considerable size, its slight tendency to secondary deposits.

All these peculiarities are, however, not sufficient to make us regard gelatinous cancer as a distinct species of cancer. The following grounds make it much more probable, that it (with the exception of the rare cancer with mucous framework, see p. 481) is no other than a common cancer in the highest stage of mucous metamorphosis :

1. The microscopical elements of the gelatinous portion of colloid cancer, and the substance of cancers which have undergone mucous degeneration, are perfectly similar : they are cells in high degrees of mucous metamorphosis, and their remains.

2. Chemical investigation demonstrates no essential differences.

3. The stroma of colloid cancer shows no difference from that of cancers which have suffered a high degree of mucous degeneration. It is sometimes distinct macroscopically, sometimes presenting cells of large size, sometimes microscopically—

distinctions which are also shown by common cancers. It is peculiarly rigid and homogeneous, contains indistinct connective-tissue corpuscles which have suffered fatty degeneration or simple atrophy, and very few vessels or is entirely deprived of vessels,—peculiarities which are explained by the considerable distention of the stroma by the increase in volume of the alveolar contents.

4. Colloid cancer and common cancer show a perfectly similar development and the same conditions of growth.

5. Colloid cancer likewise frequently occurs pure, as well as in combination with common cancer. The combination occurs in different ways: either there is present in the periphery of colloid cancer a small or broad layer of common, for the most part soft cancer; or with a primary colloid cancer there are found as secondary, sometimes colloid cancers and common cancers, sometimes only the latter.

6. The greater benignity of colloid cancer, which is evidenced by the for the most part slight secondary deposits, by its chronic course, etc., is in consequence of the destruction of the cancer-cells through mucous metamorphosis, atrophy of the stroma and especially of the vessels.

According to many, every colloid cancer is dependent upon a mucous character of the stroma, thus a mucous FRAMEWORK cancer (in opposition to the mucous CELL cancer assumed by the author). This is held by VIRCHOW and others. According to FÖRSTER, a combination of mucous framework cancer occurs with mucous cell cancer. A similar view is held by F. E. SCHULZE (*Arch. f. microsc. Anat.*, I., p. 336). According to W. MÜLLER (*Beob. d. path. Inst.*, zu Jena, 1871, p. 481) colloid development is likewise independent of epithelial elements, and is peculiar to interstitial tissue. The alveolar structure is explained by this, that only the looser connective substance ensheathing the smaller vessels is the seat of the development of mucous tissue. RINDFLEISCH (*Lehrb. d. path. Hist.*, 1873, p. 144) regards colloid substance as an accumulation and metamorphosis of amorphous formative substance. A peculiar theory of colloid cancer has been advanced by STRADOMSKY. According to RECKLINGHAUSEN and KÖSTER (l. c., p. 70), colloid cancer is also developed from the endothelium of the lymphatic vessels. According to DOUTRELEPONT (*Arch. f. kl. Chir.*, 1870, XII., p. 551), neither the cancer-cells nor the stroma furnish the gelatinous matter, but the material out of which in common carcinomata the young cells have their origin, enters under the influence of the cancer-cells into gelatinous degeneration.—Consult on the other hand WALDEYER (l. c., 1872).

CALCIFICATION of cancer-cells

occurs rarely. It affects only isolated small points, sometimes entire cancer-knots for the most part, so that these reach a consistence of stony hardness. In its lower grades it is not infrequently combined with simple atrophy and fatty metamorphosis of the cancer-cells. Thereby there arises a grayish yellow mortar-like substance, in which, besides cells which have suffered fatty degeneration and simple atrophy, there are found fat-molecules, crystals of cholesterin, simple, smoother or concentrically laminated, calcified cells and chalk molecules. (See p. 490.)

HÆMORRHAGES

occur, especially in soft and vascular cancers, especially in those of the external parts, kidneys, retro-peritoneal glands, and bones. Their importance depends especially upon the quantity of escaped blood, in part also upon its changes. Small effusions of blood into soft cancers, cause only a reddish color, like that of raspberry juice, and sometimes a greater consistence of the cancer-juice; those into hard cancers have no influence upon its farther course. More abundant and extended hæmorrhages are, on account of the resulting coagulation, followed by various degenerations of the cells, especially simple and fatty atrophy. The escaped coloring matter of the blood undergoes the usual changes. If the effusions are very large, there will arise a true hæmorrhagic cavity, which consists of blood and destroyed cancer-tissue. These cavities finally end in their drying up and the diminution of the whole cancer, sometimes perhaps in cysts, or they introduce the destruction of the cancer. The hæmorrhages, which occur on the sur-

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face of excoriated cancers of the skin and mucous membranes, as well as on
that of villous cancers, are followed for the most part by simple flowing off
of the blood and, according to its quantity, exert a varying influence on
the whole organism.

The causes of hæmorrhages lie partly perhaps in an original delicacy of the vessels,
partly in their metamorphoses.

ŒDEMA OF CANCER

occurs sometimes in cancers during general dropsy, as well as in cancers
on the extremities and in internal organs in local œdema. The changes
resemble those of other œdematous soft parts. The cancer-cells behave in
the same manner as after artificial addition of water.

SOFTENING OF CANCER

occurs sometimes as an isolated process, sometimes simultaneously with
fatty or mucous metamorphosis of the cancer-cells or with formation of pus
in the cancer. In the former case, it manifests itself, especially as cancer
of the superficial portions of the skin and mucous membrane ; as well as
the central portions of the cancer-knots in parenchymata, with a for the
most part diffuse diminution of consistence. It has its basis in an
increase, or new-formation of liquid intercellular substance, and in an
œdematous swelling of the cancer-cells. The latter become larger, more
round and spherical, the cell-membrane becomes more indistinct, thinner,
and then disappears entirely ; etc. The consequences of softening consist
especially in the introduction of decay and ulceration of the cancer.

The causes of softening are especially disturbed circulation (pressure upon and
thrombosis of the veins).

FORMATION OF PUS

is very rare in the interior of cancer, but it occurs more often on its sur-
face. It is sometimes so slight that it is recognizable only by microscopical
examination, sometimes so great that it is visible to the naked eye. It is
sometimes diffuse, sometimes there are formed abscess or cyst-like cavities,
e.g., in the mamma. The internal surface of these cysts is sometimes cov-
ered with growths like granulations.

The mode of origin of the pus, as well as its point of origin (cancer-cells or stroma),
has not yet been certainly shown.

SUPERFICIAL DECAY OF CANCER, CANCER-ULCER.

After a longer or shorter existence of cancer of extended organs, especially
of the skin and digestive mucous membrane, its surface almost constantly
decays, and there arises the so-called cancer-ulcer.

The CANCER-ULCER offers in part different characters in different organs.
The liquid covering it, its so-called secretion, resembles either common
cancer-juice, or it is serous, more rarely sero-purulent, often colored red or
brownish by blood, without odor, or with an odor which remains long on
the fingers which have been engaged in the examination of it, and which
infects the atmosphere (CANCER-ICHOR). At the same time, it often contains
particles of cancer tissue. The base of the ulcer is of very varying size and
form, according to the size of the cancer-mass and the age of the ulcer. At
first it resembles a simple erosion exposing the cancer-tissue. This increases

continuously in extent and depth, or new erosions are formed, which often coalesce. Finally, the ulcer is of a gray, reddish, greenish, or blackish color, rarely smooth, for the most part entirely irregular, superficially or deeply fissured, soft or gangrenous. The cut surface of the base and walls shows the common or somewhat softened cancer-structure. Simultaneously with the decay there grow on the base of the ulcer sometimes new, more or less villous masses, which sometimes have the character of luxuriant granulations, sometimes that of villous cancer. After a longer or shorter existence these also decay, for the most part with the immediately adjacent cancer-surface: the ulcer thereby increases in depth, quickly extends or pushes out new growths.

Most often death appears during these processes. In other cases the cancer-mass may, by excess of decay over the peripheral enlargement, be so completely separated that remains of the earlier cancer can be found only in the borders, or so completely that the ulcer resembles a simple chronic ulcer passing into cicatrization. Whether thereby a complete healing can be effected, is very doubtful.

The remaining peculiarities of cancer-ulcer depend in part upon the essential or accidental admixtures (gastric juice, remains of food, urine), in part upon the action of medicaments.

Many cases of so-called ULCUS PHAGEDÆNICUM s. corrodens of external parts as well as of the uterus, are only cancer-ulcers in which the new-formation in the base of the ulcer is very small, and sometimes only microscopically demonstrable.

Decay, in many cases, affects not merely carcinomatous parts, but also the surrounding textures.

The CAUSES of decay are: chiefly the forcing apart of the normal tissues by the new-formed cell-masses, upon which is dependent in part the enlargement of old alveoli, in part the formation of new ones; also the cancerous degeneration of the superficial tissue-layers, whereby the protecting epithelium becomes lost, and the air, secretions of mucous membranes (especially gastric juice), etc., act upon the cancer.

The CONSEQUENCES of cancerous decay are: re-dilatation of formerly contracted parts, especially important in the œsophagus, stomach, intestine; evacuation of particles of cancer: by vomiting, coughing, the stools, etc.; perforations of serous membranes (with consequent inflammation), of vessels (with slight or colossal and fatal hæmorrhages, e.g., from the aorta in cancer of the œsophagus), from adjacent hollow organs (thereby giving rise for the most part to simple, more rarely multiple FISTULÆ); marasmus, in consequence of the continuous flow of cancer-juice, in consequence of capillary and other hæmorrhages.

As CYSTIC CANCERS

are designated many, and, in appearance and origin, different forms:

1. Cancers, which are developed in cysts or cystoids, either by the cyst-wall becoming carcinomatous, or by the simultaneous formation of villous cancers of varying size and kind on the internal surface of the cyst-wall; they occur especially in the ovaries, rarely in the mamma, testicles, and bones;

2. Cancers, in which, after previous mucous metamorphosis of the cancer-cells, there occurs a formation of for the most part small, rarely of the size of a walnut, at first irregularly villous, later smooth-walled, cyst-like spaces, filled with a clear or clouded mucous liquid; carc. cysticum colloides (opposed to c. cyst. butirinicum); they are found in the stomach, liver, lungs, bones, etc.;

3. Cancers, in which some portions of the normal organ are, in consequence

of the cancer itself, transformed into cysts, *e.g.* the larger milk-ducts and the acini of the female mamma ;

4. Cancers, which show a glandular structure, and contain cavities with mucous liquid : cancroids with mucous cysts.

B. ENDOTHELIAL CANCER.

ENDOTHELIAL CANCER, in its general properties (infiltration or tumor, color, consistence, etc.), is similar to epithelial cancer, and has hitherto been almost always confounded with it. Microscopically, it shows cells which greatly resemble those of cylinder-cell cancer. The alveoli, in which these cells are imbedded, are distinguished, sometimes not essentially from those of common epithelial cancer, sometimes they are distinguished as reticular and anastomotic, and herein reminding one of a net-work of normal, very fine lymphatic vessels.

Endothelial cancer ARISES through increase of the endothelium of the lymphatic vessels, of different localities (skin, serous membranes,—perhaps also lymph-glands, testicles, brain, etc.). The endothelial cells increase, not only in number in varying proportions, but also change their form, etc., so that they become similar to cylinder- or gland-cells.

Endothelial cancer occurs sometimes pure (serous membranes, skin) ; at other times it is combined with epithelial cancer, in such manner, that a cancer proceeding from the epithelium of the skin or mucous membrane penetrates into the finest lymphatic vessels, and from here extends further. The latter appear to take place most often in the testicles and in serous membranes (*e. g.* pulmonary pleura).

RECKLINGHAUSEN (*Arch. f. Ophthalm.*, 1864, XII., p. 70) first advanced the theory that the cancroid processes were the club-shaped swollen extremities of the lymphatic vessels, and thus had their origin, that either the cell-growths entered directly into the lymphatic vessel and formed casts of it, or that a mixing of these cells with growths of the endothelium of the lymphatic vessels occurred, while an increased production of this endothelium alone could transform the lymph-roots into cancroid processes. (Consult also *Sitzgsber. d. Würzb. phys.-med. Ges.*, 1865-66). KÖSTER (*Virch. Arch.*, 1867, XL., p. 468. *Die Entwickelung d. Carcinome*, etc., 1869) has conducted these investigations farther. According to these authors, anastomoses of the cell-cylinders or cancer-processes are found in all cancers of the skin; these very often form net-works, which, in form and mode of extension, are casts of the net-work of lymphatic vessels, and in which there still often exists a central lumen. The cell-cylinders represent changed lymphatic vessels, the first cancer-cells are the more or less changed endothelial cells of the lymphatic vessels. K. goes so far as to deny a direct relation between cancer and hypertrophy of the glands and hair-follicles. According to K., colloid cancer also is most probably developed within the lymphatic vessels.

It is still doubtful whether KÖSTER's view, to this extent, is right. A certainly opposing case, recorded by PAGENSTECHER (*Virch. Arch.*, 1869, XLV., p. 490), belongs to endothelial cancer. It concerns a cutaneous ulcer, similar to cancroid, on the nose ; the finest lymphatic vessels of the skin and subcutaneous connective tissue, and the larger vessels between the muscles, were filled with epithelial-like cells, which P. derives from the endothelial cells of the lymphatic vessels. The epidermis, hair-follicles, etc., were normal.

Also, the cases described by EBERTH (*Virch. Arch.*, XLIX., p. 51) and ARNDT (*Ib.*, LI., p. 495) as epithelioma, or cancroid of the pia mater and subarachnoidal spaces, are quite positively to be included here ; also RINDFLEISCH's (*Lehrb.*, 3. Aufl., p. 614) so-called carcinoma cerebri simplex, which proceeds from the cells of the adventitia of the vessels of the pia; also CLASSEN's (*Ib.* L., p. 37), as well as PERL's (*Ib.*, LVI., p. 437), cases of epithelial cancer of the lungs, pleura, etc. Probably also many tumors of the testicles, brain, lymph-glands, etc., belong here, which WALDEYER (*Virch. Arch.*, 1872, LV., p. 67) derives from the so-called perithelial cells of EBERTH, *i.e.*, the most external adventitial cells of the vessels. They repre-

sent for the most part very soft medullary masses, which consist essentially of a vascular plexus, the vessels of which have a thick epithelial-like cell-envelope, and look like strong, anastomosing cellular pouches. Between these cell-cylinders there may be developed sarcomatous, myxomatous, etc., intervening tissue. W. calls these tumors PLEXIFORM ANGIOMATA.

Consult also ROBIN'S epithelioma of the serous membranes, GOLGI'S endothelioma (see p. 431), and KUNDRAT, Oestr. Jahrb., 1871, 2. H.

We have observed in the pleura two cases of primary endothelial cancer : one has already been published (Arch. d. Heilk., 1870, XI., p. 509); the other came under our treatment as a chronic exudation of the pleura, and at the autopsy was found to be essentially similar.

C. CONNECTIVE-TISSUE CANCER.

Connective-tissue cancer has sometimes the form of a circumscribed or diffuse tumor, sometimes that of an infiltration.

MICROSCOPICAL examination of connective-tissue cancer shows numberless cells, which are in general similar to colorless blood-corpuscles, but are not infrequently larger and contain one remarkably large nucleus, or many nuclei, or only free nuclei. The cells and nuclei lie singly or in small number in small, for the most part irregular spaces of the stroma, which are nowhere like gland-ducts. The stroma resembles, in its small number of cells, common loose or firmer connective tissue, in which are sometimes found more strongly thickened vessel-walls, or remains of the original tissue. If, on the contrary, the cells are very abundant, there is a manifold similarity with common or hyperplastic cytogenic tissue. It is for the most part very vascular.

From these characters it follows that at the present time there are no strict histological peculiarities of connective-tissue cancer, that it, especially when very vascular and deficient in stroma, cannot, or only with difficulty, be distinguished from many sarcomata, especially those characterized by round and small cells, or those which are granulation-like or lymphoid, also from many hyper- and heteroplastic developments of cytogenic tissue, from many gliomata, sometimes even from many infiltrations of pus, etc. Connective-tissue cancer stands to many sarcomata, gliomata, etc., in the same relation as glandular cancer to many adenomata. In both cases the behavior of the lymph-glands, if they are not primarily affected by the cancer, is important : their increased swelling occurs almost only in cancer of the respective peripheral parts. At the present time, the notion connected with cancer is especially clinical, not anatomical.

Hitherto all the efforts of pathological anatomists to give a precise histological character to cancer, especially to connective-tissue cancer, have been fruitless : clinical and pathologico-histological interests have not yet been united. Especially do so numerous transitions seem really to exist between the so-called benign and malignant new-formations, that a fixed limit between them is at present, and perhaps always will be, impossible. We have already made this apparent in the consideration of fibromata, myxomata, enchondromata, sarcomata, the new-formation of cytogenic tissue, adenomata. If the new-formation of small round cells in the above-mentioned tumors (on the adenomata, see p. 473) is so considerable that the type of the original new-formation is macroscopically and microscopically obliterated if the earlier, for the most part circumscribed new-formation becomes diffuse and extends to the various circumjacent tissues and organs; if in consequence of various causes the new-formation decays; if the lymph-glands become affected in like manner ; if metastases occur through breaking of the new-formation into the veins,—then they, in a clinical sense, have become cancerous.

All the characters above given hold good, more or less perfectly, of a series of new-formations, to which practitioners apply the term cancer, while the names given by pathological anatomists vary greatly. We first described a peculiar case of this kind

as "heterologous tumorous new-formation of cytogenic substance" (*Arch. f. phys. Heilk.*, 1858, p. 123; *Schmidt's Jahrbb.*, 1859, CIII., p. 109; see also *Arch. d. Heilk.*, 1865, VI., p. 44). BILLROTH'S "cancer with a structure similar to that of the lymph-glands" (*Virch. Arch.*, 1860, XVIII., p. 82) likewise belongs here. The same is true of LANGENBECK'S so-called "scrofulous sarcomata," of some cases by LAMBL and O. WEBER. VIRCHOW later (*Die krkh. Geschw.*, II., p. 728) introduced the now quite generally adopted, and in many ways ambiguous, name "LYMPHO-SARCOMA" (sarcoma lymphomatodes s. lymphaticum). The tumors described by LÜCKE (*D. Z. f. Chir.*, 1873, II., p. 199) as medullary sarcoma of the lymph-glands (most often of the axilla, of the inguinal region, more rarely of the neck, also of the region of the tonsils) likewise belong here: L. proposes therefor the name lymphoma (the latter he calls lymphoid). *Vide infra.*

HIRSCHBERG (*Der Markschwamm der Netzhaut*, 1869) has almost certainly demonstrated the identity of glioma retinæ with the medullary cancer (fungus medullaris s. hæmatodes oculi) of the older authors. Glioma advances along the optic nerve into the cranial cavity, or forward into the anterior chamber of the eye, etc., not infrequently attacks the cranial bones and the skin in the vicinity of the eyes, later the lymph-glands on the parotid and on the angle of the inferior maxilla, is the origin of metastases to the liver, etc., and often returns after extirpation. It is not infrequently bilateral.

On account of enlargement of the spleen, and often also of the lymph-glands, and on account of the general symptoms, etc., which, with exception of the increase of the colorless blood-corpuscles, resemble those of leucocythæmia, some cases are described as pseudo-leucocythæmia (COHNHEIM), others as lymphatic anæmia (WILKS).

The ORIGIN of connective-tissue cancer agrees in general with that of other cellular new-formations proceeding from connective tissue. It takes place by far most often from the corpuscles of connective tissue of every kind, and of various normal and pathological tissues.

By repeated division of the connective-tissue corpuscles there are formed at first indifferent cells, which always remain so or later acquire more determined forms. Or, by endogenous formation there arises a mass of nuclei, which soon lose their envelope of the connective tissue corpuscle; the nuclei are then transformed into cells, etc. Essentially in the same manner is connective-tissue cancer developed in osseous tissue: the basis substance of the bones, in the vicinity of the young cancer-focus, for the most part along the vessels, loses its salts and is transformed into a fibrous tissue. Probably in an entirely similar manner is the development of cancer-cells from colorless blood-corpuscles effected (in thrombi), also from the nuclei of the capillaries, of the sarcolemma, etc., as well as the so-called metamorphosis of new-formations of other kinds (fibromata, cysts, sarcomata) into cancer. In many cases cancer is developed from many tissues simultaneously.

The stroma of connective tissue cancer consists at first of connective tissue, the corpuscles of which produce cancer-cells, or of atrophic tissues of other kinds, e.g., glandular substance. Later, the stroma in many cases is formed probably from the increasing connective-tissue corpuscles.

The GROWTH of connective-tissue cancer takes place, for a small part, by increase in size and number of the old cancer-cells (by division and endogenous formation), as well as by formation of new cancer-cells in the stroma. For the most part the growth is peripheral: the immediately adjacent tissues are layer by layer transformed into cancer, entirely in the same manner as in the first formation of the cancer.

Connective-tissue cancer may present two varieties, which are for the most part strictly separable, but sometimes, even in the same case, in different organs or in the same organ, even in the same knots, they pass into one another: the hard and the soft connective-tissue cancer.

a. The HARD CONNECTIVE-TISSUE CANCER, SCIRRHUS, FIBROUS CANCER (chondroid cancer, carcinoma fibrosum, *squirrhe ligneux*, etc.—hard lympho-sarcoma).

Hard connective-tissue cancer is characterized by this, that the cut sur-face is firm, sometimes of the same consistence as the normal tissue, some-times much firmer, fibroid or cartilage-like, and creaks during section. Its color is gray, grayish white or grayish red. It is uniformly smooth, like lard, or fibrous, a little moist, juiceless, or lets exude a scanty serous liquid, or here and there, rarely throughout, a scanty milky juice. Cancers of this kind are more usually small, for the most part infiltrated; they are sometimes rounded, sometimes they present on the periphery processes of varying number and length. Their growth is for the most part slow. They occur primarily especially in the mammæ, and in the groups of lymph-glands in the neck, mediastinum, etc., more rarely in the spleen, bones, etc., secondarily in the lymph-glands, serous membranes, lungs, liver, kidneys, etc. The secondary cancers are sometimes hard, sometimes and more often soft. This form of cancer passes by increase of cells, etc., into medullary cancer; on the other hand, a medullary cancer may be transformed into scirrhus (*vide infra*).

Hard connective-tissue cancer is histologically less characteristic than the soft. Especially is a confusion possible with many atrophic epithelial cancers (see p. 489), with many tubercles and syphilomata, with atrophic lymph-gland tumors, etc. Pro-bably there belong here many cases by HODGKIN (*Med.-Chir. Trans.*, 1832, XVII., p. 68), WILKS (*Guy's Hosp. Rep.*, 1856, C. II., p. 117; 1859, V., p. 115; 1865, XI., p. 56) and others. Also the case by WUNDERLICH and the author (l. c., 1858), that by R. MAIER (*Arch. d. Heilk.*, 1871, XII., p. 148), that by LANGHANS (*Virch. Arch.*, 1872, LIV., p. 509). The new-formations of the lymph-glands and spleen are best known histologically. According to VIRCHOW and LANGHANS, these and the folli-cles of the spleen are considerably enlarged, become hard and stiff; the microscope shows an increase of lymph-cells, a thickening of the old, and formation of new reti-culum, often true connective tissue; the surrounding structures are not affected, but suffer only from pressure. Our own case was somewhat different. Especially char-acteristic is the encroachment of the structure mentioned of the part first affected on the surrounding textures, whether connective tissue, or fat-tissue, or muscular, or osseous tissue, etc.

b. SOFT CONNECTIVE-TISSUE CANCER, MEDULLARY CANCER (encephaloid, soft cancer, cellular cancer, etc.—soft lympho-sarcoma).

Soft connective-tissue cancer is characterized by its cut surface, which is homogeneous, whitish, grayish-white, or of various shades of red, and not infrequently also here and there speckled red or yellow. It is usually soft in the most varying degree, to the consistence of the fœtal brain, more rarely harder. It is perfectly homogeneous, or only here and there indistinctly fibrous. On scraping there is everywhere given off, and uni-formly, a for the most part abundant liquid, which is rarely slightly mucous, for the most part creamy or milky, increasing in proportion to the length of time elapsing between extirpation or death and the examination.

Soft connective-tissue cancer usually forms tumors, of sometimes con-siderable size. It is found in all organs which contain connective tissue, especially the loose variety, and appears always to arise from this, but then grows by substitution into the remaining portions of the organ. The localities most frequently affected are: the intermediate tissue of the various tissues, organs, and parts of organs, the subcutaneous and inter-muscular tissues, the periosteum and endosteum, the retro-pharyngeal and retro-peritoneal connective tissue, the looser connective tissue around the salivary and milk-glands, around the kidneys, the adventitia of the bronchi, the capsule of the kidneys and lymph-glands, the interstitial connective tissue of the organs last mentioned, probably also the mamma, salivary

glands, liver, lungs, muscles. Medullary cancer occurs at all ages, but especially in the first and later years of youth.

We ourselves have observed its occurrence in most of the above-mentioned localities. (More exact data are given in another place.) VIRCHOW found soft lympho-sarcoma most frequent in the cervical glands, whence it passes to the lymph-glands of the axilla and mediastinum ; also in the persistent thymus gland.

Metastases follow, according to VIRCHOW, especially to the spleen, more rarely to the liver, lungs, kidneys.

To soft cancer there likewise belongs a series of cases, which have for the most part received other names : besides those given above, by BILLROTH, the author, VIRCHOW, the case by COHNHEIM (*Virch. Arch.*, XXXIII., p. 452), EBERTH (*Ib.*, LIX., p. 63), many cases of so-called sarcoma carcinomatodes (VIRCHOW).

The occurrence together of connective-tissue cancer on the one hand, and epithelial and endothelial cancer on the other, has not yet been observed.

The metamorphoses of connective-tissue cancer, its influence on organs and on the whole organism, resemble those of cancer in general.

XIV. CYSTS, OR ENCYSTED TUMOR. CYSTOMA.

HODGKIN, *Med.-Chir. Transact.*, 1829, XV., p. 265.—KOHLRAUSCH, *Müll. Arch.*, 1843, p. 365.—FRERICHS, *Ueber Gallert- u. Colloidgeschwülste*, 1847.—BRUCH, *Ztschr. f. rat. Med.* 1849, VIII., p. 91.—ROKITANSKY, *Denkschr. d. Wien. Acad.*, 1849, I. ; *Wochenbl. der Zeitschr. d. Wien. Aerzte*, 1855.—METTENHEIMER, *Müll. Arch.*, 1850. —STEINLIN, *Ztschr. f. rat. Med.*, 1850, IX.—VIRCHOW, *Ztschr. f. wissensch. Zool.*, 1850 ; *Würzb. Verh.*, V., p. 461 ; *Verh. d. Berl. Ges. f. Geburtsh.*, 1848, III. ; *Arch.*, V., p. 216 ; VIII., p. 371 ; *Deutsche Klin.*, 1859, p. 196 ; *Die krkh. Geschw.*, I., p. 155.—LEBERT, *Gaz. de Paris*, 1852, No. 46, 51 et 52 ; *Prag. Vjsch.*, 1858, LX., p. 25.—MARTIN (and FÖRSTER), *Ueber die Eierstockwassersuchten*, 1852.—MECKEL, *Illustr. med. Zeit.*, 1852.—GIRALDÈS, *Mém. de la soc. de chir.*, 1854.—WERNHER, *Virch. Arch.*, 1855, VIII., p. 221.—BECKMANN, *Virch. Arch.*, 1856, IX., p. 221.— HESCHL, *Prag. Vjschr.*, 1860, IV., p. 36.—KLEBS, *Virch. Arch.*, XLI., p. 1.—FOX, *Med.-Chirurg. Transact.*, 1864, XLVII., p. 227.—BÖTTCHER, *Virch. Arch.*, XLIX., p. 297.—WALDEYER, *Arch. f. Gynäkol.*, 1870, I., p. 252.

CYSTS are tumors, which consist of an inclosing fibrous sac, of simple or very complicated structure, and lined by an EPITHELIUM (or endothelium) and with more or less FLUID CONTENTS. The latter easily distinguish cysts from all other tumorous new-formations ; the former are called HOLLOW tumors, in contrast with the latter, the FILLED tumors.

Therefore from the cysts are excluded : those spaces in connective tissue which are filled with serous liquid ; the cyst-like incapsulation of foreign bodies and parasites ; the cyst-like tumors, which consist of mucous tissue. BÖTTCHER (*Dorp. med. Ztschr.*, 1871, I., 4. H.) describes larger and smaller " cysts " in the spleen, which had arisen from small points of softening, dependent upon a high degree of lardace-ous degeneration of the arteries. The cyst-like cavities appearing in many tumors, the contents of which vary, but are for the most part thin, serous, or mucous, to which a special sac or cyst is wanting, likewise do not belong here ; this condition is called CYSTOID METAMORPHOSIS.

A small portion of cysts are, from their first appearance, NEW-FORMA-TIONS : properly so-called CYSTOMATA. The largest portion arise through tumorous accumulation of liquid (transudation, secretions of every kind, mucus, exudation) in natural or new-formed cavities : so-called hygroma, œdema, etc. This accumulation of liquid is dependent upon various causes, and of itself presents no peculiarity ; it gives rise to cysts only by accumulating in cavities, which are closed or later become so. Hereupon

cysts, on the one hand, pass into dropsies (*e.g.*, hydrocele, spina bifida, hydrencephalocele), on the other hand, into inflammations (many cases of hydrocele, of cerebral softening), as well as into metamorphoses (*e.g.*, mucous metamorphosis of the labial glands, colloid metamorphosis of the thyroid gland). But in the greater number of these cases there is associated with the abnormal accumulation of liquid, etc., a new-formation of connective tissue and vessels, and a new-formation, or enlargement, or change in form of the epithelial or endothelial cells. For this reason, but especially from practical considerations, it is proper to include cysts among the new formations.

Cysts which arise through new-formation, as well as those which owe their origin to a transformation of pre-existing physiological hollow spaces, in many cases differ greatly from one another, in others pass in many ways into one another.

Cysts are of frequent occurrence, and have been found in all organs and tissues.

A. With respect to the ORIGIN OF CYSTS there are distinguished :

1. Cysts which proceed from the transformation of normal hollow spaces.

The hollow spaces concerned contain, at the beginning of the cyst-formation, either a tolerably indifferent liquid (serum, mucus) which in the transformation of the hollow space to a cyst suffers only slight changes. Or their contents consist of a specific secretion, *e.g.*, milk, bile, urine, etc., or it consists of blood. This substance diminishes with the further development of the cyst and finally disappears for the most part entirely, while, at the same time, the liquid of the cyst is discharged from the vessels, or is formed by its epithelium. The cells of the epithelium remain permanent, only increased in number ; or from them complicated forms arise (glands, hair, etc.) ; or they are changed, for the most part by becoming more flat. The wall of the hollow space is thickened (urinary tubuli, bile-ducts) ; or it increases almost always in connective tissue and vessels, and loses more or less completely its original character.

a. Cysts which, through ENLARGEMENT of NORMAL, yet more or less closed, SEROUS or MUCOUS SACS : the so-called dropsy of the bursæ of the subcutaneous connective tissue (especially in front of the patella), of the muscles, sheaths of tendons (so-called ganglion, hygroma gangliodes, tumor synovialis, especially on the back of the hand, palm of the hand, dorsum of the foot), of the synovial sheaths (so-called synovial ganglion or hydrocele articularis), of the sublingual mucous glands, hydrocele vaginalis. Also cysts arising in old hernial sacs (hydrocele herniosa, hydrorrhachis externa, hydrencephalocele, etc.) belong here. Many include here also common hydrocele (accumulation of non-inflammatory liquid in the tunica vaginalis of the testicle), which is warranted only in so far as it forms a distinct tumor. In all these cases there occurs an increased secretion of liquid or a diminished absorption of it (diseases of the lymphatic vessels) or both.

Mucous sacs occupy, for the most part, an intermediate position between physiological and pathological formations. They arise most often in the superficial or deep subcutaneous connective tissue, over parts where the skin is exposed to irritations or strong frictions (in front of the patella, where not infrequently there are two mucous sacs overlying one another, over the spinous process of the seventh cervical vertebra, in front of the prominence of the thyroid cartilage, in front of the hyoid bone, over exostoses, growing bone-callus, etc.). Their mode of origin is not certainly known. They have for the most part no endothelial covering.

b. Cysts which arise through DISTENTION OF CLOSED FOLLICLES (in con-

sequence of hyper-secretion of the liquid of the follicles (so-called dropsy), or of mucous metamorphosis of the epithelium), for the most part with hypertrophy of the wall of the follicle: from the Graafian follicles of the ovaries, from which many for the most part smaller, and according to many, all ovarian cysts have their origin, and from the corpora lutea, also from the follicles of the thyroid gland, the Malpighian bodies of the kidneys, etc.

The proof that many ovarian cysts arise from the Graafian follicles, is afforded by the discovery of ova in the cysts (ROKITANSKY and others). KLEIN (*Virch. Arch.*, XXXVII., p. 504) demonstrated the origin of renal cysts from degenerated Bowman's capsules: they contained gelatinous masses of varying size, in which were fat granules, various crystals, calcareous grains, and crystals of cholesterin; the vascular loops showed various degrees of retrograde formation, often with increase of nuclei. According to RINDFLEISCH (*Lehrb.*, 1873, p. 456), congenital, sometimes very numerous renal cysts, arise from the Malpighian bodies.

c. Cysts which are formed by TRANSFORMATION OF MUCOUS MEMBRANE CHANNELS. These occur for the most part from catarrhs with consecutive contraction or complete closure of the excretory ducts; in consequence of their closure by inspissated mucus, calculi, cicatrices, etc. Here belong the so called false or sacculated dropsies: dropsy of the gall-bladder, hydrometra, dropsy of the Fallopian tubes, dropsy of the vermiform process, renal dropsy (hydro-nephrosis), dropsy of sacculated bronchiectasiæ. All these cysts at the beginning contain the common secreted matter, but later for the most part no trace of the original contents of the cavity, but usually a serous or sero-mucous liquid; the formerly cylindrical epithelium is for the most part transformed into pavement epithelium; the mucous membrane becomes like a serous membrane.

d. Cysts, which arise from COMPLETE CLOSURE OF, ACCUMULATION OF SECRETIONS within, etc., the DUCTS beyond and within the glands, or even in the acini: so-called RETENTION-CYSTS. The causes of these cyst-formations are in part pressure from without, contraction by foreign bodies (concretions, etc.), inflammation through formation of cicatrices, valvular formations; in part the causes are unknown. Here belong comedones, milia, and atheroma of the external surface of the body, which arise through accumulation of the secretion of the hair follicles or of the sebaceous glands, or of both at the same time, and through further, in part, complex processes; the rarer atheromata of the mucous membrane of the mouth, especially of the hard palate; those of the lacunæ of the tonsils; mucous cysts (or hydatids) of the longer mucous glands, especially those of the uterus, stomach, large intestine, urinary bladder, female urethra, antrum of Highmore, larynx, etc.; cysts of the bile-duct; also many cysts of the mamma (so-called involution-cysts), of the salivary glands, especially the sub-maxillary (ranula), of the glands of Bartholin, of Cowper's glands, peptic glands, testicles, kidneys, especially the pyramids and pelves, finally the rare cysts of the decidua vera. This is true of the metamorphosis of the original glandular contents and glandular epithelium as well as in c.

On the (inconstant) glands of the pelvis of the kidneys, consult UNRUH (*Arch. d. Heilk.*, 1872, XIII., p. 289) and EGLI (*Arch. f. micr. Anat.*, 1873, IX., p. 653).

c. Cysts which arise from BLOODVESSELS, especially veins, or from LYMPHATIC VESSELS (hæmato- and lympho-cystides). These contain either the former contents, or a serous liquid. They arise at one time through constric-

tions in the course of a vessel (vena saphena—lymphatic vessels of the neck), at another time through sacculated, aneurismal or varicose dilatations with final constriction of the pedicle (cranial sinus) : in both cases there follows in the constricted sac a further secretion of serum, etc.

KLEBS (*Hdb. d. path. Anat.*, p. 95) describes lymph-cysts of the skin, which proceed from dilatation and constriction of the lymphatic vessels. They were provided with a thin, membrane-like serous membrane, which was smooth, glistening and, at least in one case, covered with a flat epithelium. Later on, vascular, villous, and warty formations, which occasion hæmorrhages, may appear on their internal surface.

f. Cysts which arise in consequence of ARRESTED DEVELOPMENT OF FŒTAL ORGANS : cysts on the spermatic cord (remains of the *processus vaginalis*), those on the Fallopian tubes and in the broad ligament (remains of the parovarium, Wolffian body and duct, Müller's duct); the so-called Morgagnian hydatids on the testicles ; perhaps also the cysts occurring on the epididymis, as well as many cysts on the surface of the liver, near the *ligamentum suspensorium* (which constantly have a ciliated epithelium), the congenital serous cysts or hygromata and dermoid cysts of the cellular tissue on the neck and back.

The cysts in the first portion of the spermatic cord (so-called hydrocele cystica funiculi spermatici) arise probably from the so-called *corpus innominatum* (GIRALDÈS), a remains of the Wolffian body and analogue of Rosenmüller's organ in the female. Here belongs also the very rare origin of cysts in the urachus through further growth of the frequently persistent, broad or pedicled dilatations, or, through further growth of parts of it, remaining partially open (LUSCHKA, *Virch. Arch.*, XXIII., p. 1.—HOFF-MANN, *Arch. d. Heilk.*, XI., p. 373).

The deeper atheromata of the neck are retention-cysts of the cervical fissures :* of the second, if they are connected with the styloid process; of the third, if they are situated on the hyoid bone and the sheaths of the vessels. (Investigations of ROSER, HEUSINGER, VIRCHOW, SCHEDE.)

2. Cysts which arise from EXTRAVASATIONS OF BLOOD (so-called hæmorrhagic or apoplectic cysts).

These cysts occur, by the formation of connective tissue in the periphery of the extravasation, with or without signs of inflammation, which gradually forms an inclosed sac, on the internal surface of which there is produced no endothelium or one similar to pavement epithelium, and from which the blood is gradually absorbed, leaving behind serous contents, not infrequently mixed with the elements of the hæmorrhage, pigment granules or crystals, etc. Cysts of this kind occur rarely, most often in the brain, more rarely under the skin, between the muscles, under the periosteum (cephalhæmatoma) and perichondrium (othæmatoma), on the extremities of fractures, in the ovary (cystic degeneration of the corpus luteum), in the uterus (polypous hæmatoma), in the kidneys, etc. ; not infrequently also in the blood-coagula of the new-formed vascular connective tissue of the internal layer of the dura mater (so-called hæmatoma of the dura mater). (See p. 220.)

3. Cysts, which are PRODUCTS OF PRIMARY ORIGIN : CYSTOMATA proper.

These cysts proceed either from CONNECTIVE TISSUE, OR ANALOGOUS CORPUSCLES. The latter increase by division or endogenous growth, so that there arises a sharply defined mass of young cells. The most external cells form the capsule of the future cyst, into which vessels probably grow from the surrounding structures ; the cells immediately adjacent become the epi-

* Consult DALTON, *Human Physiology*, 1875, p. 780.—[ED.]

thelium of the cyst; the most internal, and most of the cells, undergo a
serous or colloid metamorphosis, the product of which becomes the con-
tents.   Here belong perhaps many cysts in the ovary, many cysts in gran-
ular kidney, many cysts of the thyroid gland, bones, parenchymatous
organs, etc., many dermoid cysts separated from the skin; probably a num-
ber of the cysts in new-formations (fibroma, enchondroma).

Many include in new-formation cysts also those, where in consequence of atrophy
in some places, there results a hernial protrusion of a synovial membrane or sheath
of tendons, which later grows by secretion of liquid and new-formation of vascular
connective tissue and endothelium (*kyste peri-articuiaire*—hygroma and meliceris).
Others, with equal right, include these among the cysts formed by constriction.

Or cystomata are products of TRUE EPITHELIUM.   Here belong probably
most cases of ovarian cysts.   The epithelium of the wall of a Graafian folli-
cle increases and sends into the limiting stroma protrusions comparable
to the fœtal pouches, which, by colloid metamorphosis of the central cells,
and constriction, become cysts.   The latter grow to a varying size, and then
the same process is repeated in them.

Thus most ovarian cysts arise not from common ovum-bearing Graafian folli-
cles (see p. 506), but from the more embryonic forms of the epithelium of the ovary,
similar to Pflüger's pouches, which are not transformed into normal follicles, but
from the beginning into cystomata.
According to WALDEYER, there are two possibilities, which explain the occurrence
of epithelial accumulations in the ovary of adults.   Either the first beginnings of
cystomata must be dated back to an early period of development: this is supported
by the occurrence of small cystomata already in the new-born, and the occurrence of
larger ones at a comparatively early age.   Or there still arise after the period of
fœtal life and after maturity, embryonic forms, beginning follicular formations in
the ovary: this is shown by microscopical observation.

There probably occur also many subcutaneous dermoid cysts and athero-
mata through simple inversion of the epithelium of the skin, especially
through constriction of the epidermal process forming the future hair-folli-
cle.   The atheromata are therefore to be regarded as arrested formations of
the hair-follicle.   In dermoid tumors situated at a distance from the skin,
the closing of the abdominal cavity during fœtal life becomes a matter for
consideration.

The occurrence of dermoid tumors in the ovary can be explained by this, that the
primitive ducts of the renal and sexual organs are not, as has been assumed hitherto,
derived from the middle, but from the upper germinal layer.   (HIS. *Arch. f. microsc.
Anat.*, 1865, I., p. 151.)   According to WALDEYER, these cysts are formed similarly
with those above mentioned; but the new-formed epithelium assumes an epidermoi-
dal character.
According to W. FOX, cysts arise in papillomata and epithelial cancers by the
growing together of the papillæ.

Of a series of cysts there are some, of which the origin has not yet
been demonstrated: thus of all more rarely occurring large cysts and cys-
toids, of the so-called anomalous mucous bursæ (*bursæ mucosæ præ-osseæ*)
over the spines of the vertebræ, amputation-stumps, luxated and unreduced
bones, club-feet, etc.

The same holds true of the so-called heterologous ciliated cysts, *i.e.*, those which
are found in parts, in the vicinity of which ciliated epithelium nowhere occurs: *e.g.*,

in the abdominal wall over the umbilicus, between the muscles and peritoneum, in the œsophagus, etc. (WYSS, *Virch. Arch.*, LI., p. 143.)

WINCKEL (*Arch. f. Gynäkol.*, 1871, II., p. 383) furnishes a group of cases of cysts of the vagina, and describes a *colpo-hyperplasia cystica* occurring in the pregnant state.

RINDFLEISCH (*Lehrb.*, 1873, p. 481) derives a form of ovarian cystoid from a colloid degeneration of the *stroma ovarii*. He calls it SOFTENING-CYST.

The ORIGIN OF NEW CYSTS occurs either at a distance from the old cysts, and then possesses no peculiarity; or in their wall. In the latter case, as well as when cysts are developed immediately beside one another, they often penetrate by their further growth into the cavities of the old or primary cysts, which sometimes are filled by one or many secondary cysts of the same kind. In the wall of these secondary cysts new (tertiary) cysts may again arise, etc., whereby the structure of such compound cysts becomes almost inextricable. Or cysts, which arise by side of older cysts or even in their wall, open by their further growth into the cavities of the old. If merely one young cyst be present, then there will arise a simple hole of varying size; if several or very many of these be found, the old cyst will be perforated like a sieve.

The GROWTH of cysts has in individual cases not yet been closely followed. It is usually slow.

B. THE CONTENTS OF CYSTS
vary, especially with the mode of origin, in part also with other influences.

SEROUS, MUCOUS, and COLLOID CYSTS
allow the character of their contents to be easily recognized; only sometimes are transition steps met with, between the three kinds of cysts. Besides, with the exception of the contents, they have in general similar properties.

The SAC consists of connective-tissue fibres or connective-tissue bundles, which for the most part are firmly felted to one another, within condensed into a kind of homogeneous surface, without for the most part existing as looser tissue, and of vessels in varying number. It is usually a sac easily removed; rarely, it consists of simply atrophic tissue and is not removable. In the colloid cysts of the ovary the cyst-wall consists of two distinct layers: an external dense, fibrous layer poor in cells, and a smaller, cellular, and vascular layer.

The INTERNAL SURFACE is always covered with epithelium, which exists for the most part in a single, rarely in many layers, is, with serous contents for the most part, flat and, according to the place of origin of the cyst, epithelial or endothelial in character, but, with mucous or colloid contents, is almost always cylindrical, sometimes also ciliated. New-formation cysts, the so-called cystomata, show still farther complications of structure, which are best known of the ovarian cysts. In so-called GLANDULAR CYSTOMA inversions occur into the cyst-wall, and all transitions of such inversions to true glands, and of these again to cysts. New-formed glands may likewise furnish epithelial inversions, etc. In so-called PAPILLARY CYSTOMA there arise on the internal surface of some or of all parts of it simple or arboriform, mostly vascular, papillary excrescences of varying size, which sometimes fill the whole cavity of the cyst or even break through this and grow into the abdominal cavity.

The CONTENTS of the cysts are rarely without solid constituents; they mostly contain scanty or abundant separated epithelial cells, which not in-

frequently undergo fatty, mucous, or colloid metamorphosis, sometimes single blood- or mucus- or pus-corpuscles; rarely other substances, *e.g.*, spermatozoa (hydrocele spermatica or spermatocele). The cyst-contents are sometimes only transudations, sometimes partly transudation, partly products of the metamorphosed epithelium. Many ganglions, especially those on the flexors of the fingers, contain so-called *corpuscula oryzoidea*, which sometimes arise from constricted, polypous formations of the internal surface, sometimes products of coagulation of the contents.

The contents of GANGLIONS are a peculiar, gelatinous, tenacious secretion (meliceris) ; it is neither an albuminous nor a gelatinous body, but a kind of synovial or colloid substance ; it is very similar to the soft substance which is found in the intervertebral cartilages of children (VIRCHOW). According to HOPPE-SEYLER (*Virch. Arch.*, XXVII., p. 392) the liquids of cystic goitre, as well as those of multilocular ovarian tumors show a composition varying with the size of the cavities. In the smaller, usually little or no albumen is found, but only a small quantity of a material like mucin, while the large mostly contain very much albumen in concentrated solution. The mucous contents of ovarian cysts have sometimes more the properties of mucin, sometimes those of albumen, or of par- and metalbumen (WALDEYER).

BLOOD-CYSTS,

i.e., cysts which are filled with liquid blood (not incapsuled extravasations), are very rare, occur especially in external parts, and histologically have been but little investigated.

The rare dilatations of vessels with cyst-like form, but still communicating with the vessel, as *e.g.* DEMME'S extra-cranial blood-cysts communicating with the cranial sinuses, also the small aneurisms occurring especially often in vascular tumors, finally the hæmorrhages occurring in pre-existent serous sacs (tunica vaginalis of the testicles, etc.), or in already existing cysts with contents of other kinds, do not belong here. (See p. 507.)

DERMOID CYSTS IN THE BROADEST SENSE

consist of a fibrous vascular sac, but which plays the *rôle* of the skin or derma. On this account these cysts also may be included among the newformations of the skin, which occur in form of cysts. The essential element is the epithelium on the internal surface of the sac. It is everywhere present or only here and there, resembles that of the skin of the new-born, consists of rete Malpighi and epidermis, and it undergoes continuous regeneration, whereby the thrown-off epidermal scales must accumulate in the cavity of the cyst. To this are added for the most part still further products of the internal surface of the cyst. This surface is sometimes smooth, sometimes it supports a varying number of for the most part irregularly formed papillæ of varying size. In the corium hairs also are uniformly distributed or only in places, which hairs sometimes resemble wool, sometimes the hair of the pubes, sometimes that of the head, and are almost always accompanied by sebaceous glands. These glands are found sometimes independently of the hairs. In both cases their fatty secretion likewise accumulates in the cavity of the cyst. The occurrence of sweat-glands in the cyst-wall is much more rare.

The so-called ATHEROMA, ENCYSTED TUMOR (in the narrower sense), contains a grayish white, grayish or dirty red or brownish mass, which varies in consistence, sometimes liquid, sometimes like gruel, sometimes crumbling (not infrequently with isolated small, irregularly formed, more solid lumps), after evacuation of which the internal surface appears smooth or irregularly fissured, soft or of horny hardness, homogeneous or lami-

nated. The atheromatous contents consist of epidermal cells, which are rarely normal, with or without a nucleus, for the most part lamellated, simply atrophic and much broken up, sometimes are also round, and lie separate, or are concentrically laminated ; also they consist of the abundant remains of these cells, of free nuclei, of variously abundant, fine and large fat-globules, free or still inclosed in the cells, often of crystals of cholesterin, and not infrequently of little fine hairs. The most internal portions of the wall contain the same epidermal cells in simple contact, or arranged in concentric lamellæ. Next to the fibrous membrane (the corium) there is found an arrangement and character of the cells similar to those of the rete Malpighi. The corium itself (so-called pericystium) is for the most part thin, rarely thick, usually without papillæ, but contains quite rarely, and then for the most part small, but numerous hair- and sebaceous glands. Through further metamorphoses, especially inflammation of the cyst-wall, hæmorrhages of it, calcification of its contents, these tumors may assume a varied appearance. Atheromata are situated most often in the subcutaneous connective tissue, especially of the scalp and scrotum ; in the interior of the body they are more rare. Atheromata, not infrequently occurring in the tonsils, behave in essentially the same manner.

Nearly related to atheromata is the so-called molluscum sebaceum s. contagiosum, a peculiar wart-like tumor of the skin, which arises by distention of the sebaceous glands with secretion and their projection on the surface of the skin. BATEMAN, CAZENAVE, BÄRENSPRUNG, VIRCHOW and others believe in the infectiousness of this tumor.

The so-called CHOLESTEATOMA

consists of a for the most part thin capsule and of contents which are uniform at the centre and in the periphery, pure white, shining, like stearin or spermaceti, of a fatty feeling, not liquid, and which often to the naked eye shows a lamellated arrangement. Under the microscope there is observed as the chief element of the contents very delicate, flat, for the most part non-nuclear cells, of a round or for the most part polygonal form ; these usually lie in contact and at the point of contact, often show an altogether uniform single row of small fat-globules. Besides, there often occur small hairs, sometimes also crystals of cholesterin. The sac consists of the same fibrous substance as that of atheroma, and sometimes contains hairs. Its internal surface shows sometimes a distinct rete Malpighi, sometimes no trace of it. Cholesteatomata occur sometimes in the subcutaneous cellular tissue, rarely in internal organs, most often in the pia mater of the brain.

Most probably there are many cholesteatomata which, not connected with true epithelium, are to be explained as arising from endothelial growth of the connective tissue, of the meninges, bones, etc.

FAT- AND OIL-CYSTS, DERMOID CYSTS proper, consist of a for the most part thick sac and a grayish, yellow or yellowish green contents similar to oil, butter, or solidified fat. Their wall everywhere, or in separate circumscribed points, has a cutis-like structure : it consists of epidermis, which is abundantly exfoliated and forms the contents, of rete Malpighi, and of a corium with or without papillæ, as well as of longer or shorter hairs. Besides, the internal surface shows not infrequently numerous very small openings, from which on lateral pressure there exudes a sebaceous mass. Those openings correspond to the wide mouths of the mostly very large sebaceous glands, otherwise like the normal glands, the secretion of which

together with scales of epidermis, form the contents of the cavity of the cysts; from the openings there not infrequently emerges a hair; more rarely the sebaceous glands are small and undeveloped in proportion to the hair. Sweat-glands are sometimes present in cysts of this kind, mostly in much fewer number than the sebaceous glands, sometimes they are wanting. Their structure wholly resembles that of the normal glands. Under the layer forming the corium there not infrequently lies a distinct panniculus adiposus. Many cysts finally contain in their wall cartilage, or bone, or teeth, some even warts or condylomata, or cutaneous horns. Dermoid cysts proper occur most often in the ovary, very rarely in the testicles, skin (especially in the region of the temple and eyes), pleura, lungs, mesentery, brain, uterus, etc. They are probably always congenital. They are mostly simple cysts, or concern almost always only one cyst of a compound cyst tumor. The dermoid cyst communicates sometimes with common cysts, in which case then the latter may likewise be filled with fat and hairs.

C. Number, size and form of cysts.

The number of cysts in an organ varies in the highest degree: sometimes there are found only one or a few, sometimes the organ is occupied by an infinite number of independent cysts, so that only a little of its structure is visible. In very rare cases various tissues or organs show similar cysts simultaneously.

(The author, *Arch. d. Heilk.*, V., p. 92.)

The number of cysts found in an organ is either one; or there occur several or many at the same time: so-called COMPOUND or MULTILOCULAR CYSTS, CYSTOID. In the latter case, the relation of the separate cysts to one another varies. Most often there is a principal cyst, which partly incloses many smaller cysts, secondary cysts; or the latter lie together in the wall of the former. Or the tumor consists of cysts, which stand in no such relation to one another. Between these different forms of cysts there are again transitions. Especially may a cystoid thereby at least apparently be transformed into a simple cyst, when by the growth of the principal cyst all the secondary cysts are compressed into microscopical smallness, or the secondary cysts open into the principal cyst and thereby lose their independence.

The SIZE of cysts is likewise variable: from a microscopic size to that which equals the area of the whole abdominal cavity. The greatest volume is reached by mucous and colloid cysts.

The FORM of cysts is almost always round or rounded; other forms are mostly dependent upon the surrounding solid parts, or upon the fact that many cysts arise in a small space and in their growth are mutually compressed.

D. The consequences of cysts

consist, besides, in the destruction of the tissue at the place of the cyst (especially in those of parenchymatous organs), especially in pressure on the neighboring tissues, whence sometimes inflammatory irritation of them, sometimes true new-formation of tissue (in the skin: acne punctata, a. rosacea, a. indurata, molluscum, acrochordon, nævus follicularis, etc.; on mucous membranes: catarrh, partial or general hypertrophy—acne hyperplastica colli uteri, vesicular polypi), sometimes finally simple atrophy. The clinical importance depends especially upon the size and number of the

cysts, on the importance of the mother-organs, upon the encroachment upon the surrounding structures, on some metamorphoses of the cysts. Cysts of the ovaries, of the skin, and many congenital cysts possess the greatest practical importance. Some cysts of medium size, *e.g.*, those of the ovaries, as well as numberless small and larger cysts, *e.g.*, of the kidneys, are not infrequently without any importance.

E. CHANGES IN CYSTS.

Changes of the liquid of the cysts, so far as these are connected with the life of the cyst, are naturally continual. Grosser changes of the contents depend always upon demonstrable alteration of the cyst-wall. Whether the sometimes varied contents of the separate cavities of a cystoid are primary or secondary, cannot often be decided.

Moderate hæmorrhages into the cavities of cysts with admixture of blood with the contents of the cyst and transformation of the same into pigment, render the contents, as well as to the internal surface of the cysts, pale-red, chocolate colored, or dark red. If the hæmorrhages are larger (from veins of the cyst-wall), then for the most part there appears no pigmentary metamorphosis of the blood. These hæmorrhages, usually of traumatic origin, occur especially in subcutaneous, or superficial injuries of easily exposed, for the most part thin-walled and serous or mucous cysts: the so-called hæmatoma præpatellare, hæmatocele, the so-called blood-cysts of the thyroid gland, and of the ovaries (especially with a villous character of the internal surface).

A woman was dissected by us who bore an ovarian cystoid which had been punctured about sixty times. She usually stated before the puncture whether the contents of the cyst were clear or (from hæmorrhage) were colored red. The latter was always the case, if the husband had, in consequence of domestic discord, struck her on the abdomen.

INFLAMMATION of the cysts, which is more rarely spontaneous, more often the result of accidental external influences and surgical operations, shows the usual inflammatory changes of the cyst-wall, and is often followed by a purulent effusion into the cavity of the cyst. The pus is sometimes present in small quantity, sometimes it fills the whole cavity of the cyst. The consequences of inflammation of cysts are various: rarely, inspissation of the pus with shrinking of the cyst; more often extension of inflammation to the surrounding structures, *e.g.*, the peritoneum, usually with fatal termination; or perforation of the cyst (outward, in the surrounding mucous membranes. into serous sacs).

FATTY METAMORPHOSIS OF THE EPITHELIUM of cysts, in slight degrees, is frequent and without essential importance. In its higher grades the epithelium is thrown off, whereby the contents of the cyst become streaked or uniformly grayish yellow or yellow. Also the cells of the cyst-wall may suffer fatty degeneration.

CALCIFICATION and OSSIFICATION of the cyst-wall are of comparatively rare occurrence, sometimes only in places, sometimes throughout the wall of a simple cyst, or in a part of a cystoid, and then is followed by an arrest of the growth of the cyst.

LACERATION AND PERFORATION of cysts, in consequence of external force or after inflammation of the cyst-wall; by papillary excrescences.

TURNING of cysts ON THEIR AXIS, with strangulation of their vessels, only in the *ligamentum ovarii:* in consequence of this, inflammation, hæmorrhage, etc.

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According to Rokitansky (*Oestr. med. Jahrb.*, 1865, p. 132), the turning and strangulation of ovarian tumors is not rare (8 times in 58 cases); it occurs quickly or slowly; in the first case it is often fatal, but, as it is so much more frequent in the second case, is tolerated, and undoubted spontaneous repositions occur during life; in consequence of the tolerated turning and strangulation there sometimes results involution and decay of the tumor.

Spontaneous shrivelling or decay of the cysts, whereby their walls become hard, dense and rigid, and the papillary growths of the internal surface likewise degenerate, has been observed especially in ovarian cysts of old women.

Spontaneous involution was observed by us in a boy, 3–4 years old, who had a tumor of one mamma, of the size of a goose-egg, consisting of cysts; as well as once in an ovarian cyst of the size of the first, in a dead person.

The contrary is presented by those cases, in which after one or more punctures of simple cysts there appear two or more cysts of medium size: the considerable growth of the large cyst had arrested the development of the others, which now, during the diminution of the large cyst by evacuation of its contents, proceeds quickly.

Combinations of cyst-formation with other new-formations occurs in many ways. The relations are especially complicated, if these new-formations, as is most frequent in the mamma, grow into the gland-ducts, which have been in no manner transformed into cysts.

Also there occur new-formations of other pathological tissues on the internal surface of the cysts or in the cyst-wall. There occur here, besides the already described origin of cysts in the wall of old cysts (so-called proliferous cysts) and the new-formation of papillary excrescences on the internal surface of the cysts, especially the new-formation of sarcomatous substance (see Sarcoma) and cancer (see Cancer).

XV. COMBINED NEW-FORMATIONS, MIXED TUMORS.

The terms combined or mixed new-formations may either be applied to those, which are composed of more than one tissue, *e.g.*, those of connective tissue and vessels. In this sense must here be included most of the above described new-formations, especially all tumors. Or they are those, in the composition of which there are two or more of the preceding compound new-formation or tumors. But in this consideration there are many qualifications: since, 1, *e.g.*, many cysts in new-formations do not proceed from the latter, but from the normal organs or tissues, as is frequent in the mamma; 2, since *e.g.*, an especially greater vascularity of a tumor is not always to be regarded as a combination; 3, since different stages of development of a tissue or tumor cannot be regarded as a combined new-formation; finally, 4, since it is usually impossible to decide, whether two or more different tissues have arisen at the same time, or whether one has preceded the other.

The tissues and new-formations which are most often combined, are:

1. connective tissue, common, as well as mucous tissue.

Common connective tissue determines, by its greater abundance, a greater density of the tumor, as *e.g.*, is observed in the examination of the so-called fibrous and cellular sarcomata, of soft and hard cancers (in most cases).

Mucous tissue occurs in various combinations, which have only more

recently become known : with common connective tissue, with cartilaginous tissue, cancer, etc. Especially to be mentioned here is the so-called mucous cancroid (p. 489).

2. VESSELS, which by their occurrence in large numbers, furnish the condition of the so-called teleangiectatic or cavernous degeneration of a new-formation (see p. 374).

On so-called PLEXIFORM TUMORS consult VERNEUIL, LOTZBECK, and BILLROTH-CZERNY (*Arch. f. klin. chir.*, 1869, XI., p. 230). See also VIRCHOW, *Die krkh. Geschwülste*, III., p. 257.

ARNOLD (*Virch. Arch.*, LI., p. 441) describes a myxo-sarcoma teleangiectodes cysticum of the pia mater.

A myelogenic cysto-sarcoma myxomatodes of the bones of the head is described by SCHEIBER (*Virch. Arch.*, LIV., p. 285). Consult also MODEL, *Fall. v. glandul. Cysto-sarcom mit autogenem Atherom. Erl. Diss.*, 1858.

3. CYSTS, from which arise the so-called cysto-fibromata, cysto-lipomata, cysto-enchondromata, cysto-sarcomata, cysto-adenomata and cysto-carcinomata. Most of these tumors were formerly called CYSTO-SARCOMATA, in which were included cystoids, tumors with simultaneous cyst-formation in the mother-tissue, etc. They occur especially in the mamma, testicles, and salivary glands.

In fact every tissue and new-formation may combine with others, as follows from the above description of the separate tissues. Tubercle only has never been found as an element of a mixed tumor.

Thus is it also with true mixed forms of sarcoma and carcinoma, *i.e.*, tumors, in which certain portions are sarcomatous, others carcinomatous : SARCOMA CARCINOMA-TOSUM. In cases of this kind, which occur especially in melanotic tumors, the process more rarely is by metamorphosis of the already developed sarcomatous into cancerous elements, or by their generation ; for the most part, the cancerous elements proceed with the sarcomatous from the mother-tissue, sarcoma and carcinoma grow together, like two branches of the same trunk (VIRCHOW, *Die krkh. Geschw.*, II., p. 181, 370 et 376).

Finally, those cases of tumors are worthy of notice which consist throughout of similar or different tissues. The enchondromata and dermoid cysts furnish examples of the simultaneous occurrence of tissues, which belong together. Especially striking, however, are the cases where, *e.g.*, connective tissue in its different forms and stages of development, cartilage and bone-tissue, vessels, muscular substance, cutaneous tissue, cysts, etc., sometimes even sarcomatous and carcinomatous tissues are found in the same tumor. These combined new-formations seem to occur in all tissues and organs; most often in glands, especially the salivary glands (in the parotid, submaxillary glands and their neighboring structures : combinations of enchondroma, sarcoma and myxoma), glands of generation (testicles and ovaries), the mammæ.

Combined new-formations possess in general all the properties of the several simple new-formations found in them. Their influence on the surrounding structures and on the whole organism depends, not upon the multiplicity of tissues occurring in each case, but especially upon the richness of their cellular elements (sarcomatous and carcinomatous structure).

PART FOURTH.

PATHOLOGY OF THE BLOOD.

(SO-CALLED ANOMALIES OF THE COMPOSITION OF THE BLOOD: DYSCRASIE.)

THE literature of special subjects will be found under the appropriate heads. Of general interest are the following works:

HEWSON, *Experimental Inquiries into the Prop. of the Blood*, Lond. 1774.—THACKRAH, *Inquiry into the Nature and Properties of the Blood*, 1819.—SCUDAMORE, *Essay on the Blood*, 1823.—STOKES, *Pathol. Obs.*, I., 1823.—NASSE, *Das Blut*, 1836.—LECANU, *Etudes chim. sur le sang humain*, 1837.—REES, *On the Analysis of the Blood and Urine in Health and Disease*, 1837.—DENIS, *Essai sur l'applic. de la chimie*, etc., 1838.—MAGENDIE, *Leçons sur le sang et les altérations de ce liquide*, 1838.—ANDRAL, *Essai d'hématologie pathol.*, 1843.—SCHERER, *Chem. u. microsc. Untersuch. z. Pathologie*, 1843.—ANCELL, *Vorles. üb. d. Phys. u. Path. d. Blutes*, German transl. from English, 1844.—ZIMMERMANN, *Zur Anal. u. Synth. v. Pseudoplast Process*, etc., 1840.—ANDRAL et GAVARRET, *Rech. sur le sang*, Annales de Chemie et de Physique, t. LXXV., 1840.—ZIMMERMANN, *Ueb. d. Analys. d. Blutes u. die pathol. Krasenlehren*, 1847.—POPP, *Unters. üb. die Zusammensetzung d. Blutes in verschied. Krankh.*, 1845.—BECQUEREL et RODIER, *Rech. sur la composition du sang*, 1844.—WUNDERLICH, *Pathol. Phys. des Blutes*, 1845.—SCHMIDT, *Charact. d. epid. Cholera*, 1850.—Consult also the numerous contributions of VOIT, PETTENKOFER and their pupils in the *Zeitschrift f. Biologie*, 1865–73: also recent treatises on physiology, physiological chemistry, general and special pathological anatomy and pathology.

The blood carries into tissues and organs the substances necessary to their activity, especially to their growth; and it brings away from them the surplus of these substances, as well as others which have been produced by functional activity of the parts. It constantly contains a number of the various products of metamorphosis, in various stages of their formation. It is only the arterial which (in similar animals at similar times) has an approximatively uniform composition; whereas the blood contained in veins varies more or less in composition in proportion as it comes from different tissues and organs; in some localities it possesses more or less distinct peculiarities. This is especially true of the blood coming from organs which have a clear functional connection with the blood (lungs, liver, kidneys, intestinal tube, etc.), or from those which are the seat of important functions (muscles, brain, salivary glands, etc.). In general terms the blood may be looked upon as the focus, or middle point, of all tissue-metamorphosis.

ANOMALIES IN THE COMPOSITION OF THE BLOOD occur frequently. Lesser grades of these anomalies are either unknown, or have as yet no practical

interest. The higher grades, the so-called DYSCRASIÆ, are at least partly better known as well by means of observations on living and dead human beings, as by experiments on living animals.

The chief obstacle to the study of so-called HÆMO-PATHOLOGY is the imperfection of our knowledge of the chemical composition of the blood. In spite of numerous analyses, there are yet some important substances, the so-called extractives, which have not yet been isolated, or quantitatively estimated; there are yet wanting exact determinations of the amount of albumen, serum, moist blood-corpuscles; the estimates hitherto made of fibrin are unsatisfactory; the characteristics of hæmato-crystallin are as yet but little known, etc. Furthermore, we lack an exact knowledge of the differences between arterial blood and the venous blood which escapes from various organs, of differences in blood-composition in large bloodvessels and capillaries, of variations in the fasting state and after taking food, etc. Lastly, our knowledge of the origin (except in the fœtal state), regeneration, and destruction of blood-corpuscles is very imperfect.

The anomalies of composition of the blood which have a practical interest, occur in various ways:

1. All the constituents of the blood, or one of them, are not present in normal quantity and quality; or they escape from it in abnormal quantity.

2. Certain elements of the blood are not metamorphosed in a normal manner; or they are not at all, or not sufficiently separated from the blood in the appropriate localities.

3. Injurious substances reach the blood from without.

The causes of these anomalies are either external influences (food, air, etc., — poisonous gases), or consist in diseases of various organs of the body, especially such organs as bear a relation to blood-making (spleen, etc.), or such as serve for the elimination of certain constituents of the fluid (kidneys, etc.), because these diseases interfere with the entrance of substances necessary for nutrition or respiration, or because through these diseases poisonous substances are produced which cannot be made harmless. However, it appears probable that there are not, properly speaking, any primary anomalies of the blood. If we exclude unnatural external influence, we nearly always discover that diseases of tissues and organs cause anomalies of the blood (solidistic pathology as opposed to humoralistic pathology). Nevertheless, from a practical standpoint it is provisionally desirable to admit diseases of the blood: in view of the generalization of the disorder, of the appearance of some symptoms directly or indirectly from the blood (cutaneous and urinary abnormalities, etc.), of our greatly insufficient knowledge of primary local disorders, etc.

In what follows, the various practically important anomalies of the blood will be treated of without special classification. Intoxications, properly speaking, do not belong to this section.

I. ANOMALIES OF THE SIZE AND SHAPE OF THE BLOOD-CORPUSCLES.

Pathology has as yet profited but little by our knowledge of changes in the shape and size of red blood-corpuscles. In physiology it has long been known that red blood-corpuscles assume a more globular shape and become larger in blood whose watery constituents are increased, and that removal of the gases of the blood, its treatment with alcohol and gallates, act in the same manner, while the addition of salts causes these bodies to shrink and shrivel. (For changes in white corpuscles see p. 152 and p. 357.)

Of how much importance the above changes may be, is shown by an approximative determination of the superficial area of blood-corpuscles. If it be assumed that the blood of a man amounts to 4,400 C. cent., the blood-corpuscles will collectively present a surface equal to 2,816 square metres. If 176 C. cent. of blood be thrown into the lungs every second, the surface occupied by the red corpuscles in

this quantity will be 81 square metres. (WELCKER, *Arch. f. microsc. Anat.*, 1872, VIII., p. 472.)

MANASSEIN (*Med. Centralbl.*, 1871, No. 44) has investigated the changes in dimension which red corpuscles undergo under various conditions. The following results were obtained by more than 40,000 measurements made in 174 animals. Septicæmic poisoning, and probably also traumatic fever, caused reduction in the size of the corpuscles. The same result was caused by increased temperature, and by sojourn of the animal in a space surcharged with carbonic acid gas. Means which reduced the temperature of the animal brought about an increase in the size of the corpuscles; this was true of medium and large doses of muriate of quinia, cold, hydrocyanic acid in lethal and non-lethal doses, alcohol in intoxicating doses. Muriate of morphia and oxygen enlarged the corpuscles. Acute anæmia (after arterotomy) produced the same result.

LASCHKEWITSCH (*Oest. med. Jahrb.*, 1871, p. 425) observed in a case of Addison's disease that the red corpuscles were larger, paler, and altered in shape; they appeared biscuit-, club-, or worm-shaped, and sent out a number of processes which were drawn in again; they showed constrictions, and in some places were thus separated.

MICROCYTHLÆMIA is the name given by VANLAIR and MASIUS (*Bull. de l'Acad. Royale de Méd. de Belgique*, 1871) to a disease which is chiefly characterized by the appearance in the blood of peculiar elements (microcytes). These are small elements, not exceeding .003 or .004 mm. in diameter, brightly shining, of the same color (or even deeper) as the red corpuscles; their surface is smooth, and they do not aggregate. At first, in the cases observed, their number was about equal to that of the red corpuscles, but, increasing progressively, reached the proportion of one or two of the corpuscles to one hundred microcytes. As the patients became convalescents, the microcytes were found to have disappeared, but all the red corpuscles were smaller (.006 to .007 mm.). The authors consider these bodies as intermediate forms in the process of shrinking and disappearance of red corpuscles. According to their view, the red corpuscles of the blood are not wholly destroyed in the spleen, but pass into the condition of microcytes, whose complete destruction takes place in the liver. Under normal conditions, microcytes, which after their formation in the spleen are destroyed in the liver, are not at all found in any blood but that of the vena portæ, or, if found, only in very small numbers. The authors consider the disease as due to increased activity of the spleen and diminished activity of the liver. NEDSVETZKI (*Med. Centralbl.*, 1873, No. 10) describes little bodies possessing movement in all directions (blood-nuclei, hæmococci) as constant ingredients of normal blood. These are probably identical with ZIMMERMANN'S "elementary corpuscles," LOSTORFER'S syphilitic corpuscles, etc.

II. ANÆMIA IN GENERAL.

In practice we designate as ANÆMIA several different conditions dependent upon causes which cannot always be determined exactly during life, which have this in common, that there is either a diminution of the quantity of the blood, or of the amount of certain ingredients of the blood necessary for nutrition (red blood-corpuscles and albumen). In conjunction with this there is occasionally a positive or relative increase in the amount of the remaining constituents of the blood (water, white corpuscles), so that there occurs a transformation of anæmia into hydræmia, leucocythæmia, etc.

TRUE ANÆMIA, that is to say, a condition in which the amount of blood, or the contents of the bloodvessels, is reduced, does not occur, or does so only for a very short time, after large losses of blood; because even during the hæmorrhage there is, on the one hand, a diminution in the amount of fluid given off to the tissues and lost with excretions, and, on the other hand, an increased flow of lymphatic and of interstitial (so-called parenchymatous juice) fluids into the bloodvessels, so that the water of the blood is relatively increased at the same time that its blood-corpuscles, especially the red, and its albumen are diminished.

1. ACUTE ANÆMIA, OR OLIGÆMIA.

The CAUSES OF ACUTE ANÆMIA are : abundant losses of blood after accidental wounding of arteries and veins, in large surgical operations, and by bloodletting ; a number of morbid states occurring in pregnancy, in childbed, in the puerperal state ; the so-called spontaneous rupture of arteries and veins in the interior of the body (aneurisms, perforations by ulcers, bleeding from new-formations, etc.) ; great muscular exertions, etc. (Compare p. 212.)

RANKE (see p. 173) has observed a primary reduction in the quantity of the blood after great muscular activity ; by long-continued, extreme (tetanus) muscular contraction the blood of the frog many undergo a primary reduction of 26 per cent.

The symptoms of acute anæmia are best exhibited after hæmorrhage in previously healthy persons, or in such as have been ill but a short time, and where the flow of blood externally is not prevented. In persons who have been ill some time, and where the blood is retained within the body, the symptoms are not rarely much less striking.

The phenomena are generally brought about by : on the one hand, by the diminution of the whole mass of the blood, the reduced amount of red blood-globules and albumen, as well as of the solid ingredients ; on the other hand, by diminution of the blood-pressure. Tissue-metamorphosis is nearly everywhere rendered less active ; its amount being in direct proportion to the quantity of blood.

One result of diminution of the amount of blood by hæmorrhage is that in a short time the heart and bloodvessels become positively narrower than they were before the loss of blood. This true reduction in the amount, together with the allied concentration of the blood, are soon remedied by the flowing in of albuminous parenchymatous juices into the relaxed vascular system, or by the removal of a greater quantity of the same fluid by radicles of the lymphatic system. The same result is also simultaneously favored by diminution of the amount of secretion. In consequence of such diminution of quantity there ensue certain changes in the blood : the red corpuscles are proportionately diminished, the watery constituents proportionately increased, the amount of fibrin is lessened.

The phenomena of anæmia, and their explanation are known, in part, by studies on diseased human beings, in part confirmed by numerous experiments. Compare the various treatises on physiology and physiological chemistry (MAGENDIE, DONDERS, LEHMANN, LONGET, FLINT, JR.), VOLKMANN's *Hämodynamik* ; M. HALL. *On Morbid Effects of Loss of Blood*, 1830 ; BAUER, *Zeit. f. Biol.*, 1872, VIII., p. 567.

The diminution of red corpuscles after loss of blood has been well ascertained. VIERORDT (*Arch. f. phys. Heilk*, 1854, XIII., p. 259) found them reduced to 52 per cent. in a rabbit and a dog dying of hæmorrhage. Small bleedings reduce the number of blood-corpuscles but little ; but with increased loss of blood we have a disproportionate reduction. The increase in watery constituents of the blood has also been demonstrated. WOLTERSOM (DONDERS, *Phys. d. Menschen*, I., p. 167) observed that after four bleedings of twenty minutes each, the solid ingredients of the blood were reduced to 18.6 per cent., instead of 21.7 per cent. before the experiments. Contrarily, the number of white corpuscles is not diminished, but relatively increased after hæmorrhage, because after the loss of blood more lymph, with its corpuscles, they enter the vessels, and probably also because the adhesiveness of the white corpuscles makes their escape difficult, and because superabundance of plasma is favorable to their development. After very large bleedings, the white and red corpuscles were about equally numerous in the horse (MOSLER, *Leukämie*, p. 104). The marked diminution of the fibrin has been demonstrated by BRÜCKE. Contrary assertions as to the in-

crease of this ingredient are false, being based upon the fact that watery, thin blood coagulates more quickly than normal blood.

The symptoms occurring after a single large loss of blood should be ranged in two categories: 1. The phenomena which appear immediately after the hæmorrhage; 2. Those which are produced by the consequent refilling of the bloodvessels with liquid. As has been stated, the first symptoms subside rapidly; those of the second category bear a strong resemblance to those present in slowly developed anæmia (poverty of the blood in hæmoglobulin and albumen, without emptiness of the vessels). This distinction cannot, however, at the present time be very thoroughly carried out.

Compare also the consequences of extensive congestive hyperæmia upon the vascular system, and upon blood-pressure, p. 182.

The following are the more usual special symptoms observed in anæmia produced by a considerable loss of blood.

The EXTERNAL SKIN and the visible mucous membranes are pale, often faintly translucent (in consequence of diminution of red blood-corpuscles); granulations, and even neoplasms collapse.

The MUSCULAR SYSTEM, in general, is less capable of activity, because of the loss of red (oxygen-carrying) blood-corpuscles. The external voluntary muscles of the trunk and limbs are more relaxed, the patient is feeble, hardly able to move a limb or to sit or stand (hence the old-time use of blood-letting for the purpose of favoring the reduction of dislocations and of hernia, the setting of fractures, etc.); the movements are tremulous. The same weakness is shown by the respiratory muscles; hence the voice is feeble, occasional dyspnœa (which is in greater part due to want of red blood-corpuscles, and in part is caused by nervous influence), and more rapid, or occasionally more slow respiratory movements. The cardiac muscle is likewise weakened, and consequently the heart's impulse is weak, and the heart-sounds dull; and, as a result of this condition, especially feebleness of the *musculi papillares* (as well as of relaxation of the tissue of the valves), we occasionally have a systolic blowing murmur. The involuntary muscles of the blood-vessels partake of the weakness or relaxation; and the arterial pulse, which soon after the hæmorrhage is smaller, and a little hard though easily compressed, soon becomes, as a result of the relaxation of the vessels, larger and softer. The so-called venous murmurs are at first produced by the imperfect filling of the vein with blood, and are caused later by flaccidity of the venous coats. At times there is a cramplike state of the cutaneous muscles, the relaxation of which is followed by profuse sweating (see p. 168).

The NERVOUS SYSTEM presents a series of disturbances which are the consequences of impaired nutrition by insufficiency of blood, partly because of the reduction in the number of red corpuscles, and partly probably because of diminished blood-pressure. These symptoms have been in part experimentally studied. They appear with so much the greater force as the loss of blood is the more sudden. They are characterized at first by signs of irritation, then by signs of paralysis. Anæmia of the CEREBRUM produces losses of consciousness; a tendency to syncope, especially when the patient rises; and in this posture even death may ensue. Anæmia of those parts which are posterior to the corpora quadrigemina causes only spasms or epileptoid convulsions. Anæmia of the MEDULLA OBLONGATA results in great frequency of the respiratory movements, paralysis of the

vagi, with consequent rapid cardiac contractions ; only rarely the opposite. Anæmia of the SPINAL CORD is partly the cause of weakness of the voluntary muscles, as well as of disturbances in the reflex capacity (frequently a tendency to congestion, of the cheeks for example, as well as of internal organs). (See pp. 169–70.)

General convulsions do not depend upon general anæmia, nor upon that of the brain (including the medulla oblongata), but upon the stagnation of blood poor in oxygen and rich in carbonic acid, in the cerebral capillaries ; dyspnœa precedes the spasms (ROSENTHAL). (*Vide infra*, SUFFOCATION.)

The ORGANS OF SPECIAL SENSE exhibit a number of disturbances which are the result partly of anæmia of the cerebral centres, partly of that of the terminal apparatuses : sight is usually weaker ; patients complain of darkened vision, ask for more light ; hearing is rarely dulled, more usually is abnormally acute ; the sense of smell is also occasionally in a high degree sensitive ; common sensibility is lessened.

The VASCULAR SYSTEM shows important symptoms : the pulse-rate is increased ; the speed of the blood-current lessened ; the blood-pressure diminished. The last condition is quickly remedied by the influx of fluid from the tissues into the vessels.

The increased rapidity of the pulse is in part dependent upon paralysis of the vagi, in part upon the diminished fulness of the vascular system. In morbid conditions bleeding occasionally causes a slower pulse-rate, especially in those cases in which blood-letting brings about a reduction in the accumulation of carbonic acid in the body, and causes a diminution of resistance in the bloodvessels, thus facilitating circulation (BAUER). The lessened speed of the blood, in spite of increased frequency of the pulse, has been explained by VOLKMANN (*Die Hæmodynamik*, p. 197, p. 227, 1850). The speed of the blood in a dog was found to be 280 mm. per second ; after a bloodletting of 54 grm., it was 259 mm. ; after one of 79 grm., 187 mm. ; after one of 86.5 grm., 88 mm. ; after one of 76 grm., 48 mm. The blood-pressure is diminished, as has often been demonstrated since HALES and MAGENDIE. In VOLKMANN'S dog, above referred to, blood-pressure sank from 2,106 to 1,957, 1,728, 756, 405, after the various blood-lettings. Compare also TAPPENHEIMER (*Berich. d. S. Acad. d. Wissen.*, 1872, p. 193). The increase of blood-pressure observed by NAWROTZKY (*Warsch. Univ.-Nachr.*, 1871, No. 3) disappears very quickly, according to GATZUCK (*Med. Centralbl.*, 1871, No. 53). The rapid compensation of the diminished blood-pressure is due to the fact that after bloodletting the fluids in the extravascular tissues are under a higher pressure than the liquid in the vessels, and upon the fact that during inspiration pressure in the veins is negative (BAUER).

H. NASSE (*Untersuch.*, 1871) found that after small as well as large hæmorrhages in dogs, the flow of lymph increased from 10 to 31 per cent., and when repeated bloodlettings were made, it was doubled, and even more increased. At first there was a diminution in the flow, if the coagulability of the lymph was increased. The water of the lymph usually remained unchanged in amount after bloodletting ; while, contrarily, the fibrin was much diminished, the salts a little.

The TEMPERATURE OF THE BODY is lessened, occasionally, by 1°–2° C., but nearly always returns to the normal in a few hours. Patients are easily chilled, without having actual chills. If there be fever, bloodletting causes a very temporary lowering of temperature. This is not caused by diminution of tissue-waste in the body, but by increased loss of heat produced by transitory palsy of the vaso-motor nerves.

Upon the influence of bloodletting in febrile diseases, consult TRAUBE, *Gesam. Beiträge*, 1871, II., p. 212.

In the DIGESTIVE ORGANS the mouth and stomach only show distinct

symptoms: there is usually great thirst, perhaps largely due to dryness of the pharyngeal mucous membrane; the sense of hunger is often wholly gone, but may reappear in a few days; not rarely there are observed nausea and vomiting, and occasionally dysphagia; at times active peristaltic movements of the bowels, usually constipation.

According to MANASSEÏN (*Med. Centralbl.*, 1871, No. 54), the normal proportion of acids and pepsin is changed in feverish animals, and in those who are suffering from acute anæmia, the result of abundant and repeated bleedings from an artery. In artificial gastric juice prepared from feverish animals, coagulated albumen is not worse digested, and the fibrin of ox-blood is often better digested than in a similar juice made from the healthy creature. In the artificial juice prepared from animals in a state of acute anæmia, albumen is not as well digested, fibrin nearly as well, occasionally better. The intestinal movements produced by anæmia are not (L., MAYER and BASCH) the result of the anæmia proper (reduction in size of aorta. SCHIFF and others), but are caused by stagnation of blood and its consequences. (See p. 187.)

On the side of GLANDULAR ORGANS but few certain symptoms are known: the amount of urine and of urea is increased, that of bile diminished. The number of respiratory movements is lessened, although the amount inspired remains the same, because the inspirations are decidedly deeper; it is only in very great anæmia that the volume of air inspired becomes smaller. (See p. 171.)

The so-called CHEYNE-STOKES' respiration is due, according to TRAUBE (*Ges. Abhandl.*, 1871, II., p. 882), to insufficient supply of arterial blood to the medulla oblongata.

The influence of anæmia on the DESTRUCTIVE METAMORPHOSIS of the tissues has been the object of several experimental and clinical contributions. As regards the decomposition of albumen, it seems increased both in the satisfied and the fasting state.

In BAUER'S experiments there was observed in a dog weighing about 20 kil., while being fed, within the first five days after bleeding, a daily excess of 4.8 grm. urea; before bleeding, from 32–36.5 grm. The remaining solid ingredients and the water of the urine were also increased, and yet the urine had a higher specific gravity. Similar figures were obtained in the fasting state of the animal; though in this case the excretion of nitrogen was even greater. B., as well as JÜRGENSEN, has observed the same increase in man. These results are not explicable by the entrance into the bloodvessels of albuminous parenchymatous fluid; because the increase continues for several days, and because the decomposition does not take place within the vessels, but without them. Uric acid is not increased after blood-letting (NAUNYN and RIESS). BAUER explains the greater flow of water through the kidneys in part by the rather rapid re-ascent of blood-pressure, in part to the more abundant excretion of the products of metamorphosis.

The DESTRUCTION OF FATS (investigated by means of a respiration apparatus) was lessened, at first only relatively to the increased destruction of albumen, later absolutely so; and this is true of the combustion of the fats derived from the food, as well as of that existing in the tissues or set free by destruction of the albumen. Exhalation of carbonic acid was not at first materially altered, but after a while it became reduced; the quantity of water lost, and that of oxygen absorbed, were a little increased.

According to BAUER, tissue-metamorphosis is about the same immediately after as before a loss of blood. Later accumulation of carbonic acid in the blood and tissues, and the necessary supply of oxygen, are checked by more numerous and

deeper respiratory movements (*vide* Leucocythæmia). Still later, in consequence of weakening of organs and of the loss of blood, less non-nitrogenous material is destroyed, whence less oxygen is needed and less carbonic acid given off.

In consequence of the above conditions the fat of food and that produced by the decomposition of albumen are deposited in greater quantity. The more active decomposition of albumen does not alone affect the albumen of the nutritive fluids, but that of the organs as well; hence the latter often undergo a true fatty degeneration. The greater the destruction of albumen, the more abundant the deposit of fat.

The experiments of TOLMATSCHEFF (HOPPE, *Med.-chem. Untersuch.*, 1868, 3 H.), in which it was observed that animals became fat after losses of blood, confirm the above statements of BAUER. A number of pathological observations likewise point to a connection between fatty deposit and deficiency of blood. After copious and repeated blood-letting there is often observed a considerable development of abdominal fat. Many cattle-breeders increase the productiveness of their milch cows, or the fattening of animals, by occasional bleedings. Chlorotic girls occasionally become very fat.

All these phenomena vary according to the amount of blood lost, according to the suddenness with which the loss takes place, according to individual peculiarities, according to the preceding condition of health,—even according as to whether the bleeding take place externally or internally, and in the latter case as to whether the blood is removed without mechanical help (in the cranial and spinal cavities, pericardium and other serous cavities, etc.).

The AMOUNT OF BLOOD WHICH A HUMAN BEING CAN LOSE WITHOUT DEATH ENSUING, depends upon age, sex, individual peculiarity, strength of body, state of nutrition, etc. On the average, the loss of a pound of blood will produce syncope in a grown person. Roughly speaking, in the same way, the sudden loss of a quantity equal to about one-half the total amount in the body (in grown persons four to six pounds), must be considered as sufficient to cause death. In new-born children the loss of a few ounces, and in children one year old that of half a pound, is highly dangerous. The escape of the last-named amount is of importance in old people, and in those already weakened. In general, women bear large hæmorrhages better than men. The ease with which many women bear the large loss of blood which sometimes accompanies the expulsion of the fœtus and placenta, is explicable by the fact that an organism hitherto incorporated in the female body no longer demands nutrition.

The more sudden is the escape of blood from the bloodvessels or the heart, the more severe are the symptoms, and the sooner death ensues. Fat individuals bear losses of blood less well than spare ones, the former having a smaller amount of blood than the latter. While lean rabbits show a proportion of blood to body-weight equal to 1 : 18, in fat animals it sinks to 1 : 30 (Ranke). Animals killed by the acute anæmia produced by hæmorrhage die asphyxiated, inasmuch as, in consequence of want of oxygen produced by sudden diminution in the number of red blood-corpuscles, there occurs over-irritation and consequent paralysis of the respiratory centre in the medulla oblongata. By means of a fresh supply of red corpuscles charged with oxygen this over-irritation may be reduced to the normal irritation, and respiration be set going again directly through the medulla oblongata, and not in a reflex way through the vagi (EULENBURG and LANDOIS).

Small and medium losses of blood are, as is well known, often produced for therapeutical purposes by means of leeches, wet-cups, phlebotomy; the former more usually in diseases of parts lying not far under the surface of the body, phlebotomy in affections of internal organs, more especially in common congestive or inflammatory hyperæmia of the brain, lungs, etc.

One local effect of bloodletting is, that the blood-pressure of the part from which the bleeding occurs is lessened or even abolished. Blood flows through the opening which comes from neighboring veins, and even from veins lying nearer the heart in so far as their valves will allow of backward flow. In the next place, the circulation in adjacent veins, and also that in the entire vascular system, is made more rapid. If, while the crural vein of a frog is open and blood flowing from it, the web be watched under the microscope, an increased rapidity of circulation is seen. According to facts above mentioned, it is likely that therapeutic bloodletting diminishes the amount of blood, and the hyperæmia, only for a short time. Venesection causes a diminution of hyperæmia also in distant organs; for example, venesection in the arm lessens hyperæmia (mechanical as well as congestive) of the lungs, brain, etc. whether this takes place directly by diminution of the amount of blood, or indirectly by an influence (centrally or by reflex action) upon vaso-motor nerves, is not ascertained. In a similar way venesection may reduce over-filling of the cardiac cavities. Respiration is diminished by venesection in pulmonary affections, but increased in cerebral diseases, in which normally it is small. This sudden healing effect is only to be expected in cases of pure congestive hyperæmia; in inflammations, in which various forms of exudations have made their appearance, bleeding has no such marked influence upon the exudation itself, but may possibly prevent its further formation by lessening the hyperæmia.

The RETURN TO THE NORMAL STATE in acute anæmia occurs, if the causes cease to operate and no complications arise, in a few weeks usually. Increased absorption of fluid from without (thirst), and from the tissues, restores water to the blood, and makes it more dilute (HYDRÆMIA). Poisonous substances, placed upon wounds or under the skin, affect the organism more quickly. Later the fibrin, albumen, and the other solid ingredients of the blood are gradually restored by the use of food; the salts are most quickly replaced. At the last, restoration of the red blood-corpuscles occurs; so that OLIGOCYTHÆMIA, diminished amount of red corpuscles, is the last to remain.

The development of red blood-corpuscles, not yet certainly known in the physiological state of adults, most probably takes place in the following manner: at first colorless cells from the spleen (its pulp and from the epithelium of the veins), from lymphatic glands, perhaps also from the lymphatic vessels, and the serous membranes, accumulate in great numbers in the blood, and in it are transformed, usually more quickly than under normal circumstances, into red blood-corpuscles. In this transformation the colorless cells become colored, reduced in size and flattened, while simultaneously their protoplasm becomes homogeneous, and lastly their nucleus disappears after a preliminary granular degeneration.

This notion, first advanced in its entirety by KÖLLIKER (*Zeitsch. f. rat. med.*, 1846, IV., p. 112), has received further confirmation by the investigations of FUNKE (*idem*, I., p. 172) and ERB (*Virchow's Archiv*, 1865, XXXIV., p. 138). According to the last-named author, the development of red corpuscles with transition-forms becomes more evident from the second to the fourth day after large losses of blood in previously healthy men. The time required for the thorough regeneration of the blood, until the process of new-formation of red corpuscles shall have returned to within its limits in normal blood, amounts to about three or five weeks. GOLUBEW'S results (*Wien. acad. Berich.*, April, 1868) are similar. RECKLINGHAUSEN (*Arch. f. micr. Anat.*, 1866, II., p. 137) observed in frog's blood a development of red corpuscles out of white cells occur in 11–12 days, and this even out of the frog's body if the blood was received in well-heated porcelain capsules, and preserved in a large glass vessel which was daily filled with moist air. Very similar, on the whole, are the views of KLEBS (*Virchow's Archiv*, XXXVIII., p. 190), EBERTH (*idem*, XLIII., p. 8), BÖTTCHER, and NEUMANN; views founded partly upon observations made in cases of leucocythæmia.

The numerous experiments upon extirpation of the spleen are partly in favor of the existence of a blood-producing function in this organ. After its removal there has been found, frequently though not constantly, a true hypertrophy of the

lymphatic glands. Apart from this, the extirpation was borne without symptoms. (Researches on animals by FÜHRER and LUDWIG, STINSTRA, VULPIAN, EBERHARD, SCHIFF, SIMON, and others; recently MOSLER, *Die Leukämie*, 1872, p. 31.)

MOSLER also observed alterations in the marrow of the bones. According to NEUMANN (*Arch. der Heilk.*, 1869, X., p. 68) there occur in the bone-marrow of adult animals and man, certain cell-forms which are identical with the embryonic germs of red blood-corpuscles; N. has advanced the hypothesis that during the whole of life there takes place a continual transformation of lymphoid cells into colored blood-corpuscles. By some preliminary experiments N. supposes that after loss of blood there takes place an increased flow of bone-marrow cells into blood-vessels, as well as an increased transformation of these cells into red corpuscles. NEUMANN (*Berl. klin. Wochenschr.*, 1871, No. 4) discovered in the liver of human fœtuses from three to eight months old a structure similar to that of bone-marrow and spleen; the connective tissue in these organs appears as a coarse reticulated tissue with numerous lymphoid cells imprisoned in its meshes, and it not merely accompanies the portal vein as a sheath, but extends far out into the tissue of the lobules (acini), so that the hepatic parenchyma between the capillaries of the acini is not exclusively made up of hepatic cells, but includes also a large number of lymph-corpuscles. In the new-born these cells are wholly absent. (Consult also *Arch. d. Heilk.*, 1871, XII., p. 186.)

The new-formation of blood-corpuscles in the inflamed cornea has been described by CARMALT (STRICKER); see p. 375. HEITZMANN (*Wiener med. Jahrbb.*, 1872, pp. 347 and 354) has seen blood-corpuscles appear in the cavities of inflamed bone and in the cells of inflamed cartilage: the first rudimentary masses of these cells he called hæmatoblasts.

According to SCHKLAREWSKI the renewal of the cellular elements of the frog's blood takes place, as is usually believed, from pre-existing elements of the blood. S. thinks that the morphological contributions of other organs are both inconstant and insignificant.

According to BÉCHAMP and ESTOR (*Comptes-rendus*, 1870, LXX., p. 265) blood-corpuscles are not simple cells, or even cell-like bodies, but are an aggregation of microscopic organisms—microzymes. These authors saw a blood-corpuscle decompose into a number of these microzymes while under the microscope, while by the same means of observation they saw a number of these bodies unite to form a colorless blood-corpuscle.

The reproduction of the FIBRIN occurs in the course of about forty-eight hours (PANUM'S researches on transfusion).

TRANSFUSION OF BLOOD consists in the injection into the veins of whipped venous blood (thus deprived of its fibrin and carbonic acid), made for the purpose of repairing the dangerous anæmia produced by large losses of blood, prolonged suppuration, etc., until the time when the lost blood shall have been reproduced by means of food, and by the hæmopoietic organs.

SUBSTITUTION OF BLOOD consists in the alternate withdrawal of a certain quantity of blood which has become altered in composition (as for example through loss of blood-corpuscles in chronic anæmia), or which has been temporarily poisoned by carbonic oxide for example, and supplying of normal defibrinated blood taken from a similar animal.

Transfusion of blood, for the elucidation of a number of physiological questions, has frequently been the object of experimental physiological investigation; and it, as well as substitution, has been employed in a number of cases of disease in man with success. In the earliest times (J. DENIS, 1667) the blood was transferred directly from the bloodvessels of one animal into the other's; later this was done by means of syringes, etc. DUMAS and PRÉVOST (*Bibl. univ. de Genève*, 1821), and also J. MÜLLER (*Handb. der Physiol.*, 1844, I., p. 124) and others, observed that defibrinated blood possessed the same qualities as that with fibrin, and that by whipping the blood (removing all its fibrin by coagulation) the danger of blocking up of blood-vessels was obviated. The first-named authors furthermore demonstrated that the blood of one vertebrated animal is under certain circumstances poisonous for verte-brates of another order or family.

PANUM (*Virchow's Archiv*, XXVII., pp. 240, et 433) showed that it is possible to remove and renew the entire mass of blood in an animal, at least up to within 3 per

mille, by the use of whipped blood, without causing much disturbance in the functions of the organism (nervous and muscular activity, nutrition, digestion, respiration, production of heat, excretion, etc.); and that transplanted (from another animal) blood remains as active as the normal blood, and undergoes decomposition just like it. Foreign, transplanted blood in the vascular system of another kind of animals is quickly destroyed, and is thrown out, in a state of solution, into the parenchymas and the serous cavities of the body, as well as excreted by the kidneys and intestinal canal.

ACUTE LOSS OF LYMPH has been experimentally shown to prove fatal more rapidly than an equal loss of blood: reliable observations on this point upon man do not exist.

Quiet dogs in the fasting state die after large quantities of lymph have been withdrawn from them; according to LESSER when the loss of lymph is equal to one-quarter or one-seventh of the volume of blood in the animal. On the contrary, the loss of even a larger quantity of blood does not cause a fatal issue. The coloring of the blood is rendered more intense by the loss of such large amounts of lymph. In such a case, HAMMARSTEN found in the blood so very great a quantity of oxygen in the blood as twenty-four per cent. It is probable that the loss of large amounts of saliva (and bile also, LEHMANN) has the same effect in fasting animals. Contrarily, no matter how much urine and perspiration are separated there is no alteration in the composition of the blood, for these excretions continue only as long as the water, salts, and urea are supplied to the blood as fast as excreted. The removal of large quantities of lymph causes an increase of the blood-pressure, whether because blood richer in corpuscles finds more resistance in the capillaries, or whether because altered composition of the blood irritates the walls of blood-vessels, is not determined. (LESSER, *Arbeit. aus d. Phys. Anst. zu Leipzig*, 1872, VI., p. 94.)

2. CHRONIC ANÆMIA.

Chronic anæmias are classified, according to their causes, into three categories.

a. CHRONIC ANÆMIA FROM DIRECT OR INDIRECT LOSS OF BLOOD, OR OTHER FLUIDS.

Its CAUSES are: 1. Oft-repeated small losses of blood, the so-called secondary hæmorrhages after operations of all kinds (see p. 217); hæmorrhage from the nose, air-passages, stomach and intestinal canal, urinary passages, sexual organs (in ulcers, new-growths, etc.); in abortion, etc.; hæmorrhage in the connective tissue, in serous sacs, etc.; in scorbutus; hæmorrhage from parasites (so-called Egyptian chlorosis, see p. 125). 2. Long-continued loss of various fluids, albuminates in particular, prolonged lactation, unusually large flow of milk, child-bearing in rapid succession, large loss of albumen in albuminuria (2–10–25 grm. in twenty-four hours), and in dysentery, fever, blennorrhoeas of all sorts, chronic diarrhoea, suppuration (especially in the bones), upon cutaneous ulcers or those upon mucous surfaces; profuse sweats, etc.

LEUBE (*Med. Centralbl.*, 1869, No. 39) has noticed the appearance of albumen and even of serum-albumen in the sweat of four patients. Long-continued muscular quietude reduces the amount of blood (RANKE).

The above include those cases in which the loss of blood and fluids does not last too long, in which the digestive and respiratory organs are in a nominal state, in which there is the possibility of obtaining plenty of nutritious food; conditions in which chronic anæmia does not usually develop, but it does appear when opposite conditions prevail.

The phenomena of chronic anæmia are more or less fully explicable by the state of composition of the blood. This alteration is in part like, or similar to that present in acute anæmia produced by hæmorrhage, or there exists a special poverty in red blood-globules (oligocythæmie) and in albuminoid bodies (hydræmia), because the other elements of the blood are relatively quickly replaced. The lack of albuminoid bodies leads to the development of œdema and anasarca, which are wanting in acute anæmia. (*Vide supra.*) Owing to a variety of causes the blood-pressure is diminished.

RIESS (*Arch. f. Anat. Phys., u. s. w.*, 1872, p. 237) found in all those cases of impaired nutrition which are called anæmia and cachexia, numerous small, glistening, white granules in the blood. They were rounded, sometimes a little angular, measuring .0007 mm. to .0015 mm.; devoid of color; and between these bodies and unchanged white corpuscles there occurred many transition forms. Chemical reactions also indicated such a relationship: by the addition of water these bodies gradually became less dense, more quickly under the influence of dilute alkalies, etc. R. considers these corpuscles to be the products of disintegration of white globules. This would explain the absolute diminution of red globules which is observed in these morbid states.

The MOST IMPORTANT SYMPTOMS are the following: General paleness of the external skin and of the mucous membranes; translucency of these parts in consequence of the diminution of parenchymatous fluid, and therefore lessened thickness; a feeling of weakness and prostration; small frequent pulse and weak cardiac impulse; the heart is irritable, hence a great tendency to congestion of internal and external organs. Respiration is calm during rest, but movements cause a more rapid increase of frequency than in health; dyspnœa appears. The temperature is usually a little lowered. Disturbances of the nervous system, although not wanting, are not as prominent as when anæmia is quickly produced: in general there is feebleness in the cerebral and sensorial functions, with abnormal irritability of the organs; the latter condition being especially marked. On the side of the digestive apparatus we often note thirst, and anorexia. Nutrition in general is lowered. The fat gradually disappears, very seldom does it remain in normal amount, or increase (*vide*, p. 522). On those parts where lesions exist, or on which pressure is made, ulceration and gangrene are easily produced.

In many cases of chronic anæmia there is a more or less well-marked hæmorrhagic diathesis, or even distinct scorbutus.

All the above-named symptoms of chronic anæmia, when present in a minor degree, are not distinct; while some of them are not distinct even in great anæmia, and physician and patient may well overlook them: this is more especially true of dyspnœa. (Consult TRAUBE, *Ges. Beitr.*, 1871, II., p. 1034.)

b. CHRONIC ANÆMIA BY LESSENED SUPPLY OF FOOD: SO-CALLED INANITION-ANÆMIA.

The most clearly defined anæmias of this class are those which are produced by HUNGER; that is to say, by absolute want, or imperfect supply of food. Inasmuch as, contrary to what was formerly thought, there is no marked diminution of blood in these cases, they are better called, not anæmia, but inanition-anæmia, or inanition.

Food is a mixture which is fully capable of maintaining the proper composition of

the body; this mixture is consequently nutritious. A substance is nutritious which furnishes elements needed for the composition of the body, or makes possible the formation of such elements.

The conditions which arise in the hungry and the starving states have been quite well studied by means of experiments on animals. In these experiments the animals were either left wholly without food, or with an occasional supply of water until death; breathing was in nowise interfered with. In man there are a number of examples in which more or less complete and uncomplicated inanition occurred; in some cases by deliberate intention, more usually because of certain diseases, stricture of the œsophagus, etc. Yet special investigation in such cases is wanting.

The questions of the quantity and kind of food are important for the individual and for the State, but equally important for the physician; partly because many diseases can be wholly prevented by a careful superintendence of diet, especially in the case of nurslings and young children, in educational establishments, orphan asylums, prisons, barracks, in countries afflicted with famine; and because many conditions which come under the physician's observation are not the results of disease, but of relative or actual inanition. Consult CHOSSAT, *Rech. expér. sur l'inanition*, 1843; COLLARD DE MARTIGNY, *Magendie's Journal de Phys.*, VIII.; BIDDER and SCHMIDT, *Die Verdauungssäfte u. der Stoffwechsel*, 1852; VALENTIN, *Repertor.*, III.: HEIDENHAIN, *Disq. crit. et exper.*, 1857; PANUM, *Virchow's Archiv*, 1864, XXIX., p. 241; VOIT, *Zeitschr. f. Biol.*, 1866, II., p. 307; PETTENKOFER and VOIT, *idem*, 1869, V., p. 369; BOUSSINGAULT, PLAYFAIR, THOMSON, SCHUCHARDT, EDWARD SMITH.

COMPLETE INANITION AS STUDIED EXPERIMENTALLY IN ANIMALS.

After the commencement of starvation the weight, functional activity, and excretions of the animal diminish. The diminution in weight is tolerably uniform during the whole duration of inanition, though during the first few days it is a little greater owing to the loss of the last food taken in. Decrease of excretions (carbonic acid, urea, etc.) is naturally less and less each day, because of the diminished weight of the body. The decrease in the functional activities, which is closely connected with decrease in the excretions, shows itself in animals during a state of rest by diminution of temperature, of the frequency of the pulse and respiration, by lessening of blood-pressure.

The excretions are supplied by waste of the body itself. Individual parts of the body do not lose weight proportionately to the loss experienced by the whole body. There are variations in the amount of the different substances excreted. The urinary secretion in the first few days diminishes much more than the body-weight, later in an equal proportion, in the last stages much more again. The excretion of carbonic acid diminishes at first in proportion to the body-weight, later less, and at the last much more again. The urine is more acid during starvation : its proportionate quantity of sulphuric and phosphoric acids increases. Chlorides diminish, and even disappear in a few days. The amount of urea excreted generally grows less and less as inanition progresses, because with lessened metamorphosis in the tissues there is less decomposition of albuminates. In uncomplicated inanition, as early as the fifteenth day, albumen and very often mucin are found. In starved animals there may be total absence of glycogen in the liver.

The greatest alterations in secretions are met with in starved herbivora; and all starved animals must become in one sense carnivora, inasmuch as they subsist on their own bodies.

The following tables of PETTENKOFER and VOIT represent, in figures, the above-named results of inanition.

It is to be remembered that a grown man, eating moderately, consumes, in twenty-four hours, 120 to 137 grm. of dry albuminous substance, 70 to 120 grm. of fat, 350 to 400 grm. of carbo-hydrates.

In the following experiments, using moderate diet, the amounts were : 137 grm. of albumen, 117 grm. of fat, 352 grm. of carbo-hydrates.

The excretions, with such a diet, during three, or two different days (twenty-four hours), were as follows (in man) :

DURING STARVATION, AND WHILE QUIET.

Urine C. cent.	Solids grm.	Urea grm.	Ashes grm.	NaCl grm.	SO₃ grm.	PO₅ grm.	Uric acid grm.
1197.5	49.5	26.8	19.7	14.6	——	——	——
907.9	44.1	26.3	18.9	13.2	——	——	——
792.6	46.3	25.0	14.4	8.5	1.72	2.95	0.55

WITH MODERATE DIET, WHILE QUIET. (31.6 GRM. OF DRY FÆCES.)

1343.1	64.5	37.2	18.1	11.4	2.56	——	0.8
1119.3	——	35.4	——	10.6	——	——	——
1367.0	63.7	37.2	20.5	13.1	2.66	4.19	0.8

WITH MODERATE DIET, WHILE ACTIVE.

1182.8	66.8	36.3	21.1	13.3	——	4.15	0.82
1261.1	66.9	37.3	19.4	12.4	2.5	4.07	0.9

DURING STARVATION, AND WHILE QUIET.

Carbonic acid exhaled. C. cent.	Oxygen inhaled. C. cent.	Water exhaled by lungs and skin. C. cent.	Total water given off. C. cent.
209.5	779.9	828.9	1976.3
197.6	742.6	814.1	1677.5
333.2	1071.3	1778.5	2524.8

WITH MODERATE DIET, WHILE QUIET.

275.7	709.0	828.0	2189.5
288.0	919.1	1009.0	2187.1
284.3	866.9	957.4	2387.5

WITH MODERATE DIET, WHILE ACTIVE.

374.7	953.9	2042.5	3219.9
336.3	1006.1	1411.8	2700.0

As regards individual organs and parts of the body, it appears that those parts which exert but little functional activity in the starving organism waste much more rapidly, as, for example, the fat-tissue, spleen, testes, etc. Weighing the various parts of starving animals has shown that the tissues and organs diminish in the following proportions :

The FATTY TISSUE undergoes the greatest waste, 91 to 93 per cent. of it disappearing ; leaving only its stroma.

Next the MUSCLES, which lose 42 per cent. ; those which are inactive fall away more than those which are active.

The BLOOD (contrary to older teaching) does not notably diminish relatively to the mass of the body, and there is nearly as little alteration in the relative amount of its important constituents : only the solids and the (especially) albumen of the serum, that element of the blood which is par-

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ticularly to be considered as nutritive material, diminish in a moderate but constant degree.

The BRAIN does not at all decrease in weight; hence in starving creatures the cerebral faculties are often unimpaired for a long time. The spinal cord and nerves diminish very little.

The fat which is stored up in fat-cells is of great importance as a reserve food in inanition, as it is consumed in this condition just as the albuminous elements of the food are, and is of equal value. The ultimate consumption of the fat is the cause of the great increase in the decomposition of albumen, which goes on until the want of albumen produces death. Individuals poor in albumen and fats, reduced persons so-called, soon die if exposed to starvation. (VOIT.)

The above statements, in opposition to the views of CHOSSAT, BIDDER-SCHMIDT, and others, have flowed from the experiments of VALENTIN, HEIDENHAIN, and especially PANUM, upon the state of the blood in inanition. The number of blood-corpuscles is not greater in well-fed animals than in starved ones; though the serum of those well-nourished is richer in solid constituents, and especially in albuminous substances. (PANUM.)

According to VALENTIN and R. WAGNER, in starved animals the red blood-corpuscles become smaller.

DEATH by inanition ensues when the animal has lost a certain part of his body-weight. The amount of this loss, and the length of time required, vary according to the species of animal, as well as according to its condition at the time the experiment is begun. Fattened animals need a certain time in order that their body-weight may approximate that of animals which are only sufficiently fed.

According to CHOSSAT, young lean pigeons die after having lost one-third of their weight (three days); old and fat ones only when they have lost one-half their weight (after thirteen days). BIDDER's cats died on the eighteenth day, at which time their body-weight had sunk from 2464 grm. to 1267 grm. According to CHOSSAT the higher animals lose from two-thirds to one-third of their weight before inanition causes death. On the average the daily loss of animals is 4.2 per cent., or one twenty-fourth of their weight each day.

MANASSEIN (Med. Centralbl., 1868, No. 18) observed in all starved animals an extreme fatty degeneration of the heart, kidneys, liver, and of cartilage in a less degree. The changes in the voluntary striped muscular fibres was analogous to that seen in typhoid fever. In perfectly fresh corpses the blood was liquid, dark, and contained gas-bubbles in variable amount. The changes in the weight of various internal organs were different: the greatest loss in the spleen (amounting even to one-half), the liver, intestines; moderate loss in the stomach, lungs, testes; while the relative weight of the supra-renal capsules, eyes, heart, brain, etc., was increased. The TEMPERATURE of the starved animals remained normal (about 39° C.) until the last three or four days; occasionally it sank to 38° C., and in the evening rose to 40° C. Rapid falling of the body-heat from 38° to 30° C. was observed by M. only in the last twenty-four hours. During the entire period the acid urine contained varying amounts of albumen, and an abundance of mucin; renal tube-casts, hyaline or granular, in large number, usually; occasionally distinct fat-globules. FLEMMING (Virchow's Archiv, LII., p. 568) found frequent and abundant nucleus-proliferation not only in the fat-cells of inflamed tissues, but also in simple atrophy caused by withholding food.

INCOMPLETE INANITION ACCORDING TO EXPERIMENTS ON ANIMALS.

a. INCOMPLETE INANITION IN THE QUANTITATIVE SENSE.

This consists in that the food given contains all the elements which enter into the composition of foods (albuminates, fat or carbo-hydrates, gluten, water and salts), though in absolutely small quantities. The phenomena resemble those of absolute starvation, but are more slowly developed.

Whereas in absolute starvation the number of blood-corpuscles relatively to the other constituents of the blood as well as to the body-weight, is hardly altered, perhaps increased, the long-continued action of incomplete inanition affects blood-corpuscles very destructively. After inanition has ceased, when nutritious food is again supplied, a condition appears in which the body-weight has again reached the normal point, in which the blood as a whole has regained its former volume, but in which the blood is deficient in blood-corpuscles, because owing to the absence of any reserve corpuscles they must be formed anew, a process much slower than that of building up the masses of the tissues and the blood. In this way is explained the fact that ill-fed individuals have a blood deficient in red blood-corpuscles. (PANUM.)

b. INCOMPLETE INANITION IN THE QUALITATIVE SENSE: *i.e.*, deprivation of single articles of food.

This leads usually just as quickly to a fatal result, although the emaciation is less.

The food of animals may be divided in three classes: albuminous bodies (plastic elements), carbo-hydrates with fats (respiratory elements), and salts.

ALBUMINOUS SUBSTANCES constitute the most important foods; they are the seat of metamorphosis, from them the tissues are formed, and they are the agents for the absorption of oxygen.

CARBO-HYDRATES (sugar and starch) and FATS serve chiefly to the production of heat, and of vital force, and may reciprocally serve in each other's place; and, furthermore, the substitution of albuminous substances for them is theoretically, and to a certain degree practically, possible. While albuminous bodies (red blood-corpuscles) carry oxygen, they are themselves decomposed, and about 80% of the albumen which circulates in the fluids through the tissues (the so-called movable, or stored-up, or circulating albumen) is thus destroyed; while only about 1% of that which is laid by in the organs, or fixed albumen (so-called stabile or organ-albumen), undergoes decomposition. Increased absorption of oxygen and increased excretion of urea are the usual consequences of increased ingestion of albumen. The importance of SALTS consists in that they form important constituents of tissues.

According to FICK (*Archiv f. d. ges. Phys.*, 1871, V., p. 40), the amount of albumen in the body is a very constant one, and the albumen of food is for the least part absorbed as such, *i.e.*, in an unpeptonized condition, and for the greatest part is used by the tissues not as albumen, but in the shape of various products which result from its complicated splitting up in the intestinal canal. According to F., the result of absorption of digested albumen is not simply an increase of the albuminous substances stored up in the economy, but the appearance of entirely new combinations in the animal fluids—the PEPTONES or their nearest derivatives, which undergo metamorphosis much more easily than common albumen. This view is very different from the one generally accepted; but according to it, the sudden increase in the excretion of nitrogenous products of metamorphosis in a few hours after a meal rich in albumen, is no longer paradoxical.

A certain quantity of the above substances constitutes a minimum for the maintenance of the body. If, for example, an adult man needs in the normal state 120--140 grm. of dried albumen, 70–120 grm. fats, 350–400 grm. of carbo-hydrates, the same man cannot subsist on about 60 grm. of albumen, and the above-named amounts of fats and carbo-hydrates. His activity and condition of nutrition vary with the amount and composition of his food. If an animal be regularly nourished with a quantitatively and qualitatively sufficient food, there shortly appears what is called the equilibrium of nitrogen (*Stickstoffgleichgewicht*), that is to say, it excretes with its urine and faeces just as much nitrogen as it takes in with its food. This balance is not destroyed by muscular activity, but only by a change in the

quantity and quality of the food.   In inanition more nitrogen is excreted at the beginning, but in a few days this amount becomes constant; the so-called starvation equilibrium of nitrogen is established, the animal subsists upon the stabile or organ-albumen, while at the beginning it lived upon the albumen remaining from food, the movable, stored-up, or circulation-albumen. In the state of starvation the amount of accumulation of circulation-albumen is very small, not equal to 1% of the organ-albumen.   Fat arrests the destruction of albumen, by keeping oxygen away from it, or by allowing the entrance of less oxygen in the blood.   Certain things act in an opposite manner, increasing the decomposition of the circulating albumen; such are: abundant drinks of water, common salt, fever.   Just like fat, sugar lessens the absorption of oxygen and thus saves albumen.   Later, sugar preserves the fat.   Starch acts in just the same manner, which, as is well known, does not become active in the organism under its own form, but as sugar. Yet it takes 2–3 parts of sugar and starch to act as efficiently as 1 part of fat.   Gluten serves in the same way.

In a state of inanition, in which the organism, after the consumption of the circulation-albumen, is obliged to make use of the organ-albumen, the tissues are no longer bathed in a fluid poorer in albumen than they are themselves; consequently, for each element which is lost by interchange between cells and plasma, a certain portion of the organ must be dissolved.   If the fat is consumed in starvation, the destruction of albumen is increased.   A true fatty metamorphosis of albumen-holding organs does not occur in simple inanition, as the moderate excretion of nitrogen indicates. Consult the well-known researches of VOIT.

COMPLETE DEPRIVATION OF WATER, including that contained in organic foods (although some animals need not drink at all, or at any rate do not drink when eating under normal conditions; as rabbits, cats), is followed by the refusal of solid food, so that death ensues as quickly as in complete starvation.

COMPLETE DEPRIVATION OF SOLID FOOD is soon followed by refusal of water, with the same result as in complete deprivation of water.

DEPRIVATION OF ALBUMINOUS FOOD (food to consist of fat and water, or of fat, carbo-hydrates and water).   The general emaciation is less, the excretion of urea is much lessened, and oxidation of the nitrogenous elements of the body made less active.

DEPRIVATION OF FAT does not produce any marked change in metamorphosis of tissues if the food contain carbo-hydrates; but if the carbo-hydrates are wanting, emaciation is moderate, the excretion of urea is much increased, and there also occurs increased oxidation of nitrogenous elements in the body, so that much more albuminous material must be ingested. These facts are explained by the knowledge we now have that fats and carbo-hydrates may be formed from albuminates.

An animal may subsist upon albumen and the salts appertaining to it, because carbo-hydrates and fats exist pre-formed, in a certain degree, in albuminous substances.   In animals or man, increased consumption of albumen is followed by an increase in the excretion of nitrogen, phosphoric acid, etc., by the urine. (J. RANKE, VOIT.)

DEPRIVATION OF SALTS is known only by the effects of the withdrawal of common salt from the food; and this is not of much importance, because unsalted foods contain as much chloride of sodium as the organism needs. Salt added to food must be looked upon as only a condiment.

Food rendered as free as possible from salt is soon rejected by animals, and they die before hunger forces them voluntarily to eat such food. Forcible feeding with substances nearly free from chloride of sodium, consisting of sufficient quantities of albumen, fat and starch, demonstrates that animals (pigeons, mice, dogs) at first excrete large quantities of salt from the body, later much less. Tissue-metamorphosis in the body goes on normally as before. After prolonged feeding, digestion becomes disordered, as is shown by the animal rejecting food in 3–6 hours, in only a slightly altered state. Analysis of the tissues and blood shows that salts are retained with great tenacity, as organs show only a very slight diminution in the amount of their solid constituents. Scorbutus never occurs; but there is noticed extreme paralysis of the muscles of the hinder extremities, and those of mastication, which only disappears after a week's feeding with salted food.

SIMPLE FEEDING WITH SUGAR causes death usually in eight days, and an average daily loss of weight of 3.4%.

SIMPLE FEEDING WITH FAT causes a great loss of body-weight (daily loss of 2.8%), and a diminution of fat, and leads to death nearly as rapidly as complete inanition.

SIMPLE FEEDING WITH GELATINE and gelatine-giving substances is likewise insufficient for the support of the body.

ANÆMIA OF INANITION IN MAN often occurs, but is seldom as purely developed as in the above-mentioned experiments. It is seldom perfect in a quantitative or qualitative sense, because usually the taking of small amounts of liquid food is possible. It is not possible to state in figures the point at which the body reaches the minimum of nutrition, because the general constitution, the condition of the digestive organs, and other factors, enter into the problem. The better the body is nourished, the more food is needed. Anæmia of inanition is seldom acute, if we exclude the hunger of ordinary life; it is usually sub-acute and chronic; in the first case it is often complicated, with fever especially.

In human beings not having fever, acute inanition is seldom observed, except in cases of insanity. I had an opportunity of studying this condition for several days in a mentally healthy person, having an abscess of the upper larynx (WAGNER, *Arch. d. Heilk.*, 1873, XIV., p. 92).

ACUTE ANÆMIA OF INANITION IN FEVER, which only relatively seldom becomes chronic, because in chronic fever the appetite is usually preserved, is caused by the usually complete loss of appetite, nearly always accompanied by thirst. This loss of appetite is not explicable. Possibly it is determined by a great diminution of gastric juice (most probably when the loss of water through the lungs and skin is great), or by qualitative changes in this fluid.

The phenomena of this anæmia of inanition differ in several respects from the kinds of anæmia already studied, in that with diminution of body-weight there is an increase in the excretions. This is caused by an actual increase in tissue-metamorphosis, hence oligocythæmia and hydræmia. The evaporation from the skin is often decidedly increased, even in those parts of the skin which feel perfectly dry. An increased separation of carbonic acid is met with in the pulmonary exhalation. The amount of urine is in general diminished, but the amount of urea, of uric acid, and of phosphoric acid, is increased. Chloride of sodium is the only element which is constantly diminished. Patients emaciate as in ordinary starvation, but more rapidly, and notably they show greater muscular weakness. (*Vide* FEVER.)

CHRONIC ANÆMIA OF INANITION appears in newly-born and young chil-

dren by insufficiency of food (too small quantity, bad condition of the mother's or nurse's milk, as well as in artificial feeding); in these, and also in adults, by severe affections of the mouth, pharynx, stomach, and intestines, which interfere with the taking of food, or at any rate, of solid food; by diminished absorption of elements of food by bloodvessels and lymphatics (various affections of the stomach and of the small intestines); by excessive corporeal or cerebral efforts and excitations, sleeplessness, pain, etc., in which cases loss of appetite constitutes a middle term. Many insane refuse all food, or will not take it in sufficient quantities for a long time. Some patients having disease of the stomach do the same from fear of pain, etc. In many non-febrile diseases of the lungs, heart, abdominal glands, the brain-inanition is produced in the above way, or through means not yet fully known. A number of forms of chronic poisoning (by lead, mercury, arsenic, malaria, etc.), lead to the same result.

The phenomena of chronic anæmia of inanition are essentially the same as those which appear in starved animals. The body-weight, functional activity, and the excretions gradually diminish, with regularity; the decrease in various organs is in the main as above stated; conditions which naturally do not prevent the development of new tissues (hypertrophy of organic muscular fibres above stenosed (narrowed) apertures, tuberculosis, cancer, etc.). The blood and excretions are more especially affected by this decrease: the urinary secretion, and the excretion of carbonic acid gas (probably) are lessened. Constipation is the rule.

The most striking and reliable numerical results are obtained from a study of the excretions of UREA. An adult, receiving a normal amount of mixed food, excretes from 30 to 40 grm. of urea. RANKE found that on the second day of inanition, it was 17 grm. SEEGEN, in almost complete morbid inanition of long standing (in a woman), determined that only 6.1 grm. were separated in twenty-four hours. SCHERER, in an insane person who had starved himself for several weeks, noted a daily excretion of urea still amounting to 9.5 grm. RANKE excreted, while taking food as usual, 9.0 grm. of CARBON, and only 7.5 grm. while fasting.

In many cases, especially in convalescence from severe acute diseases, there appears a special tendency to the separation of water; this may already happen when the blood contains six per cent. of albumen. Usually the œdema affects only dependent parts of the body (hydrops gravitatirus). (Vide infra.)

It is comparatively rare that death is produced by pure inanition. Healthy men can withstand hunger and thirst but little more than a week, very seldom two weeks; though the insane can fast longer. If water be had in abundance the fatal issue may be put off to the fiftieth day. In the various conditions referred to above, death is usually hastened by complicating diseases, in some cases by pneumonia, which may be caused by fragments of food lodging in the bronchi; or death may be the direct result of the primary disease.

INCOMPLETE NOURISHMENT CONSIDERED IN A QUALITATIVE SENSE does not occur in man in such a degree as to cause very serious results. In spite of the unsuitableness of the food used by different classes of people, by nations in various zones, there usually arises no peculiar general diseases, if no indigestible articles have been eaten, and if there have been no actual want of food. On the other hand, this imperfect feeding tends to develop a predisposition to disease, and often diminishes the resistance-power of the body to disease.

The eating of too much potatoes, and other vegetables, or other substances containing but little nitrogen, without a sufficient amount of albumen as

compensation, makes the body poorer in albumen and fats, and richer in water. This last (watery state of the body) is also produced by overwork.

c. Chronic Anæmia of unknown causation.

The types of anæmia belonging to this class are clinically well known, their diagnosis is usually easy, and in many of them certain lesions are also found after death; but their immediate cause is wholly unknown.

a. Chlorosis.

By the name chlorosis we sometimes designate a morbid condition which follows diseases which produce usually pure anæmia (so-called symptomatic chlorosis), and sometimes an independent anæmia, appearing under peculiar conditions, and accompanied by greater or lesser diminution in the number of red blood-corpuscles (the so-called pure or true chlorosis). We shall only consider the latter in this place.

The blood of chlorotic persons shows as an important peculiarity, a diminution of red blood-globules which is usually considerable (*oligocythæmia rubra*); the proportion of red corpuscles, normally from 120 to 130 per mille, may sink to 50 and less. The white corpuscles either undergo no change or are somewhat diminished. Albumen and fibrin are also present in normal quantity. The water of the blood, in proportion to the reduced number of red globules, appears increased (*plethora serosa*). The total amount of blood is usually not altered.

DUNCAN (*Wien. Sitzsber*, 1867, LV., p. 416) found in two cases of chlorosis (and one of leucocythæmia) the coloring power (depth of color) of the blood, as compared with that of healthy blood, to be 0.30, 0.31, and 0.37 : 1. The enumeration of red corpuscles showed no diminution (20,000 in healthy blood to about 20,000 in the patients); and D. concludes that diminished number of red corpuscles cannot be the most important cause of the chlorotic color, but that the reason of it lies in the fact that each blood-corpuscle contains less red pigment. In some acutely sick individuals it was found that a C.cent. of blood contained the coloring power of six millions of red globules; while in chlorotic girls, in patients with confirmed phthisis, in those having leucocythæmia, a C.cent. of blood had the coloring power of only two millions corpuscles.

QUINCKE also (*Virchow's Archiv*, 1872, LIV., p. 537) found the amount of hæmoglobin much diminished in the blood of chlorotic patients. In one case it was reduced quite to one-third of the normal amount (5.3 : 14.4); though after the use of iron during ten weeks it had quite doubled in quantity. In this case the number of red globules was distinctly diminished, and they sank more rapidly.

The conditions which determine the appearance of chlorosis are: in the first place, the female sex, and the age between fourteen and twenty-four years; bodily and mental strains; sexual excitement; occasionally unfavorable hygienic conditions with respect to food, dwelling, etc.; perverted education. The immediate causes of chlorosis are unknown. Probably it does not consist in a sudden disintegration of blood-corpuscles, but in an insufficient new-formation of white corpuscles, and a too scanty transformation of these into red corpuscles.

The ANATOMICAL STUDY of a few severe cases of chlorosis has showed, as a frequent lesion, congenitally deficient formation of the heart and large arterial trunks ("hypoplasie" of VIRCHOW); the former is at first rather small, later undergoes hypertrophy; the aorta is strikingly narrow, its walls are very thin, there are often anomalies in the origin of its branches, and wave-like or bar-like elevations of the

membrana intima, and extensive fatty degeneration of the same membrane (VIR-CHOW). According to ROKITANSKY, there is frequently incomplete development of the sexual organs, small ovaries containing only a few follicles, infantile uterus, etc. In childbed there occasionally occurs a valvular endocarditis, which, on account of its endangering life so much, VIRCHOW calls *endocarditis maligna.* Consult ROKI-TANSKY. *Handb. der Path. Anat.*, 1846, I., p. 558, 1844, II., pp. 418, 485; *Lehrbuch*, 1856, II., pp. 262, 337. VIRCHOW. *Gesam. Abhdl.*, 1856, p. 494; *Wien. med. Wo-chenschr.*, 1857. No. 27 ; *Deutsche Klinik*, 1859, No. 23 ; *Beitr. z. Geburtsh.*, u. s. w., 1872. I., p. 323. H. SCHULZE, *Ueber Chlorose*, Berlin. Diss., 1868.

The phenomena of chlorosis are pre-eminently the result of the poverty of the blood in red corpuscles (oxygen-carriers). Among them are : the pale color of the skin and mucous membranes, especially of such portions as naturally are highly colored by blood ; weakness of the voluntary muscles (sense of fatigue, indisposition to exertion, etc.), and of the heart (small, soft pulse, dilatation of the heart, murmurs in this and in the veins in consequence of abnormal tension of the cardiac valves and of the walls of vessels); shortness of breath, especially during physical exertion (with pro-longed expiration) ; weakness of the stomach and loss of appetite (in conse-quence probably of alteration of the gastric juice), inertia of the bowels (frequent constipation) ; abnormally light, pale urine, deficient in urea ; frequently scanty and pale menstruation, or complete amenorrhœa, seldom menorrhagia. It is not unlikely that to the same cause are also due the anomalies in the nervous functions (hyperæsthesia, neuralgia, cramps, hys-teria, etc. ; palpitation of the heart, tendency to rapid action of the heart, to congestion, etc.). With all the above symptoms the deposit of fat about the body often remains unchanged or even seems increased (*vide* p. 523), whereas the muscular system usually diminishes notably.

Usually chlorosis ends in cure, even without the causes ceasing to act, by the giving of preparations of iron and of fatty food. Very seldom, and usually through complications, it causes death.

In chronic heart-disease of long standing (especially common valvular lesions (there is produced a condition of the skin and of the composition of the blood similar to those existing in chlorosis, the so-called *cachexie cardiaque* of ANDRAL. The constant cyanosis of the mucous membranes serves to establish the diagnosis. The morbid condition is produced by lessening of the force of the heart, by lowering of pressure in the arterial, and increase in the venous system; by consecutive changes in the liver, spleen, kidneys, stomach, intestines, lungs, which disturb hæmatopoïesis, diges-tion, respiration, etc. ; and probably also by peculiar pigmentation of the skin. In these cases also the blood is poorer in red corpuscles and richer in water.

β. ADDISON'S DISEASE.

In this disease, besides a general extreme anæmia, there are observed a peculiar bronzing of the skin and visible mucous membranes, a special sense of weakness, etc. The important alterations found *post mortem* consist of inflammatory changes in the supra-renal capsules and cœliac plexus.

Consult ADDISON, *On the Const. and Local Effects of Disease of the Supra-renal Capsules*, Lond., 1855.—BROWN-SÉQUARD, *Arch. Gén.*, Oct. and Nov., 1856.—HARLEY, *Brit. and For. Med.-Chir. Review*, Jan. and April, 1857.—AVERBECK, *Die Addison'sche Krankheit*, 1869.—ROSSBACH. *Virchow's Archiv.*, L., p. 591, LI., p. 100.—RISEL, *D. Archiv f. klin. Med.*, 1870, VII., p. 34.—ROSENSTEIN (*Virchow's Arch.*, 1872, LVI., 27) found in two cases of *morbus Addisonii* an important decrease in the daily excretion of urea (13 to 20 grm.), and, in accord with AVERBECK, a marked

increase in the quantity of indican (64 to 75 mgrm. in 1,000 C. cent. of urine,—eleven or twelve times more than normal).

[Consult also: I. E. TAYLOR, *On the Sunburnt Appearance of the Skin as an Early Diagnostic Sign of the Supra-Renal Capsule Disease, New York Journal of Med.*, 1856, Sept.—E. H. GREENHOW, *Lectures on Addison's Disease, in Med. Times and Gaz.*, 1875, March, April, May, and June.—ED.]

BIERMER (*Corr.-Bl. f. schweitz. Aertze,* 1871, II., No. 1) describes a peculiar form of " progressive pernicious anæmia," whose development is accompanied by fatty degeneration in the circulatory apparatus (heart and small vessels), by capillary hæmorrhages in the skin, retina, brain, etc., by chronic diarrhœa.

CHRONIC ANÆMIA occurs in many diseases of the spleen, etc. See LEUCOCY-THÆMIA.

The ANÆMIA OF OBESITY has already been referred to. See Ranke, p. 378.

III. CHANGES IN THE AMOUNT OF HÆMOGLOBIN IN THE BLOOD.

HÆMOGLOBIN (hæmatoglobulin, hæmatocystallin), the ferruginous red pigment of blood-corpuscles, which holds in chemical combination oxygen, carbonic oxide, oxide of nitrogen, and which is easily decomposed by acids (even the weakest), alkalies, etc., into an albuminous body (GLOBULIN), and a ferruginous pigment (HÆMATIN), is but little known pathologically. Concerning changes in it in various forms of suffocation, *vide infra*.

The following important data are extracted from the investigations of PREYER, especially those of SUBBOTIN, *Z. f. Biol.*, 1871, VII., p. 183. The blood of full-grown animals contains more blood than that of the young. Diseases often bring about a decrease in the quantity of hæmoglobin. In a diabetic girl there was 11.1 per cent. hæmoglobin instead of 13.2 (PREYER). After large hæmorrhages and in chlorosis the reduction may go to 5 per cent., 4.6 per cent., and even lower. The great diminution of hæmoglobin in disease does not depend upon local or general starvation of the organism, for a dog starved during thirty-eight days still showed 13.33 per cent. of this substance, compared with 13.80 per cent. on the first day of the experiment. Starved herbivora (rabbits) even exhibited an increase of hæmoglobin ; while eating their usual food the proportion was 8.85 per cent. ; after fourteen days of starvation, 9.50 per cent. Quite different from the results obtained in complete inanition are those observed during the giving of insufficient food, by which the blood (and body generally) is made over-rich in water, as observed by BISCHOFF and VOIT, during the feeding of herbivora with bread. It follows from the researches of SUB-BOTIN that the kind of food used has great influence upon the amount of hæmoglobin. A food deficient in albumen, or much non-nitrogenous food, or the accumulation of fat in the body, reduces the amount of hæmoglobin. In fat animals the blood, positively diminished in quantity, contains relatively less hæmoglobin than in those less fleshy (RANKE).

IV. CHANGES IN THE AMOUNT OF ALBUMEN IN THE BLOOD.

(HYPALBUMINOSIS AND HYPERALBUMINOSIS.)

INCREASE and DECREASE of the albumen in the blood are practically of great interest. Their occurrence is by no means hypothetical, since the quantitative estimation of albumen can be very exactly made; naturally only relatively to a given amount of blood, not to the whole mass of the blood.

Albumen, which, as is well known, is taken up by blood from nitrogenous articles of food, has two important functions : 1, it is the most important substance for the nutrition and growth of tissues and organs ; 2, it possesses endosmotic properties, the fluid part of the blood having, because of its contained albumen, the property of taking up weak solutions from the stomach, intestines, and parenchymata as well, according to the laws of

endosmosis. If there be a decrease of albumen, its place will be taken either by water or salts (especially chloride of sodium), in the proportion of eight to ten parts of albumen of the serum to one part of salts (mingled as is usual with blood-salts).

1. Hypalbuminosis.

The amount of albumen in the blood may decrease from 80 per mille to 70, 50, and even 37 per mille. At the same time there occurs an increase in the amount of salts, and especially of water in the blood ; the latter rising from 905 per mille to 920, 940, and even 950 per mille. Hence the word HYDRÆMIA is often used as synonymous with HYPALBUMINOSIS, although it may be applied in other conditions, as, for example, in relative oligocythæmia. Hypalbuminosis is usually relative.

The causes of hypalbuminosis are : complete want of food, or insufficient food in the quantitative or qualitative sense.

During inanition the total amount of blood is not diminished much more proportionately than the mass of the body ; the solid constituents of the blood are not much altered from the normal ; it is only the solid ingredients of the serum, albumen in particular, which constantly diminish, though not in a striking manner (PANUM). Naturally the same result is produced by food which is quantitatively deficient, or is lacking in albumen.

Disorders of gastric and intestinal digestion act in the same manner, for, in consequence, food is not taken, or the digestion and absorption of what is taken is rendered difficult or altogether prevented ; this being the result of primary and secondary diseases of these parts, such as occur in severe febrile conditions ; severe acute diseases of all kinds ; severe affections of the liver, spleen, lungs, heart, mechanical ascites, etc. ; morbid losses of albumen by hæmorrhage of all kinds, as well as by escape of albuminous fluids (albuminuria, albuminous stools, as in dysentery, excessive lactation, long-continued suppuration, large transudations or exudations, etc.), are followed by hypalbuminosis as soon as the quantity of food ingested is not sufficient to replace the lost albumen. Of greatest practical importance in this connection is ALBUMINURIA, i.e., the escape of albumen through the kidneys. This most often occurs in consequence of change in the blood-pressure, either in the renal vessels alone (congestive hyperæmia, vide p. 181 and p. 186), or in those of the whole body, more particularly in its lower half (in severe febrile diseases, universally lessened pressure from cardiac weakness, suffocation, chronic cardiac diseases). Alterations in the parenchyma of the kidneys may be present (in all prolonged cases) or absent. Or else albuminuria is caused by true disease of the renal substance (the so-called second stage of Bright's disease, lardaceous, granular kidney ; more rarely other renal diseases). Or, it is of unknown origin (as in diphtheria, scarlet fever, etc. ; refrigeration, burning). It is questionable if besides this albuminuria of renal origin there is one of hæmic origin (as in experimentally produced dilution of the blood by injections of water, the withdrawal of chloride of sodium, by injection of albumen in the vessels). The albumen which is excreted through the kidneys is usually serum-albumen, seldom paraglobulin, paralbumen, etc. The amount of albumen excreted in this way varies in different cases from one to two to twenty and twenty-five grm. in twenty-four hours. Quantities not exceeding five grm. are not of importance in this connection.

In the so-called second stage of Bright's disease, that of inflammatory swelling of the kidney, the quantity of albumen lost in the urine is much larger than in the granular kidney; in the former the albumen may amount to three per cent. (and more), which is equivalent to twenty grm. (and more) per diem, while with the contracted kidney the albumen may not even equal as much per mille. (BARTELS.)

VOGEL and NEUBAUER (*Analyse des Harns*, 1872, pp. 267–8) estimate that in uncomplicated (by fever, etc.) cases, and in a normal state of the digestive organs, a daily loss of ten grm. of albumen can be replaced by the ingestion of three ounces of meat.

Consult BARTELS in VOLKMANN, *Klin. Vorträge*, 1872, No. 25; *Mitth. f. d. Schlesw.-Holst. Aerzte*, 1872. 4. H., p. 41.

HÆMOGLOBINURIA, that is to say, the passage of urine containing blood-pigment (though without blood-corpuscles), and showing the spectrum lines characteristic of hæmoglobin, occurs in similar circumstances.

[For loss of concealed blood-pigment in urine, consult G. Harley, The Urine and its Derangements. Lond., 1872.—ED.]

That in loss of albumen through the kidneys in nephritis not only the serum suffers, but that also the solid ingredients of blood-corpuscles are lessened, was shown by QUINCKE's investigations into the amount of hæmoglobin contained in the blood (*Virchow's Archiv*, 1872, LIV., p. 537). In several cases of nephritis with varying degrees of œdema, there were found in 100 grm. of blood, 8.5, 10.3, 11.4 grm. of hæmoglobin, instead of the normal amount, about 14.4 grm.

The phenomena and consequences of hypalbuminosis are: 1. Disturbances of endosmosis and exosmosis between the blood on the one side, and gastric and intestinal contents, parenchymatous fluids on the other. In consequence there is diminished absorption of nutritive material from the digestive tract, and thereby an increase of hypalbuminosis; and also increased or more easy escape of the liquid of the blood into tissues, hence dropsy (*vide* p. 234). 2. Insufficient formation of digestive fluids (of stomach and intestines, the bile, etc.). 3. Altered nutrition and repair of tissues. From the above conditions there appear later changes similar to those observed in chronic inanition, (*vide* p. 533), and, especially often, albuminuria.

2. HYPERALBUMINOSIS.

Although we know pretty well the quantity of albumen which the blood generally contains, we are as yet wholly without exact data upon the questions of variations in the amount of albumen in various physiological conditions (before and after eating, at different ages, after the use of different articles of food, etc.). For these reasons we cannot now consider a minor degree of hyperalbuminosis as pathological.

The diet of English pugilists, that used in the training of race-horses, aims to render the body poor in fat and rich in circulation-albumen by the giving of an almost exclusively albuminous food. (VOIT.)

Hyperalbuminosis is relative or absolute. RELATIVE HYPERALBUMINOSIS occurs in consequence of conditions by which the blood loses, simultaneously, much water and salts, and little or no albumen: as in cholera, more rarely in other diarrhœas, after the giving of drastic purgatives. It is probable that this relative hyperalbuminosis cannot long remain, because the blood quickly takes up water (in consequence of the colloid properties of albumen) from food and drink, as well as from the tissues. In this manner relative hyperalbuminosis disappears, or absolute hyperalbuminosis is established.

ABSOLUTE HYPERALBUMINOSIS, *i.e.*, the increase of the whole of the

albumen in the blood, is not as yet demonstrable, because we do not exactly know the total quantity of blood in the body. Its causes are probably a very great abundance of proteinaceous food with simultaneous small amount of muscular exertion, and feeble respiration.

V. CHANGES IN THE AMOUNT OF WATER IN THE BLOOD.

The amount of water in the blood, in its corpuscles as well as in the plasma, normally varies according to age, sex, kind of occupation, and more especially according to the kind and amount of food. During the period of digestion it is diminished, whereas all other constituents are increased. The reverse is the case in the fasting state. Long-continued eating of meat lessens the quantity of water, while a vegetable diet increases it. Abundant drinks do not augment it, or do so only temporarily, as the extra fluid is quickly excreted. The blood immediately after prolonged muscular exertion appears poorer in water than in a state of rest.

1. DIMINUTION OF THE AMOUNT OF WATER IN THE BLOOD.

A diminution of the water of the blood is observed after the action of purgatives, after severe common diarrhœa, dysentery, and especially cholera, owing to abundant transudation from the blood into the intestines; it occurs also in experimental or therapeutical water-starvation. In cholera the blood may be so much deprived of water that it assumes a tar-like consistency. At the same time the serum becomes richer in albumen and salts, particularly in potassa salts and phosphates. The latter derive from the blood-corpuscles, which are consequently impoverished, and probably in part perish. Later, the blood becomes richer in urea, owing to more or less complete arrest of the excretion of this body by the kidneys, and in spite of a certain amount of excretion by the skin. Other products of decomposition (sugar) are present in larger quantities.

Immediately after muscular exertion the blood contains a smaller percentage of water than during a state of repose, because the products of muscular waste at first accumulate in it. In deprivation of food, or when the amount of food is insufficient to replace the great waste attending labor, the muscles and the entire organism become richer in water, and ultimately the blood becomes so too. Thus it appears that excessive work produces the same effect as prolonged loss of fluids. Above all, the amount of water in the blood stands in direct relation to that in the tissues: the more water is contained in the latter, the more there is in the former. (SCHOTTIN, RANKE.)

The phenomena and consequences of diminution of the amount of water in the blood are dependent: in the first place upon this diminution itself; next upon lessened humidity of the tissues, the blood quickly absorbing their water (even serous effusions of long standing may thus be taken up); lastly, upon a secondary alteration in the circulation. Through a combination of the above conditions there appears in typical cases a characteristic group of symptoms, which we see especially well-marked in the first, so-called asphyxial, stage of Asiatic cholera.

The other consequences of diminution of the water of the blood are: great thirst, whose sudden gratification is often followed by vomiting; diminution of all secretions (urine, saliva, cutaneous exhalations, milk); collapse of external parts of the body, especially of the skin and subcutaneous fat: the skin appears wrinkled, loses its elasticity, so that its folds

remain longer in one position than in the normal state; the nose becomes
pointed; the eyes are much sunken. Muscular pains, and the frequent
local cramps are probably due to the same cause, or more particularly by
concentration of the body-fluids.

Besides, there are a number of conditions which are in part the direct
result of the reduction of the water, and in greater consequences of retarda-
tion of the circulation. This retardation is chiefly owing to diminution of
the intercellular liquid of the blood, which produces a relative increase
in red blood-corpuscles; in part, probably, due to changes in the physical
and chemical properties of the red globules (the cyanotic hue of the skin
being due to their deeper color); lastly, to secondary disorders of the nerv-
ous system. The skin and visible mucous membranes are colored gray or
grayish; the temperature of the skin is much lowered: we have the so-
called ALGID STAGE. The pulse gradually disappears, first in smaller arte-
ries, then in larger ones, lastly in the heart. In consequence of retarded
movements of the blood in the pulmonary capillaries, the expired air con-
tains less carbonic acid; patients experience sensations of oppression.
The entire muscular system is the seat of fatigue; the voice for this reason
is toneless. There not rarely appear peripheral muscular cramps, as well
as hiccough, which are perhaps produced by free potassa salts in the serum.
The proper brain-functions remain normal; there is usually complete con-
sciousness, rarely syncope; there are frequent complaints of darkened
vision, of *tinnitus aurium*. Reflex excitability is, as a rule, diminished.

If a frog be allowed to sit a long time in a concentrated solution of chloride of
sodium, or if this be injected subcutaneously, a well-marked cataract is formed
(Kunde). Is this in consequence of withdrawal of water from the crystalline lens?

The return to the normal state in mild cases usually quickly takes place
by the taking in of large quantities of fluid. In severe cases this is made
difficult, because the liquids are again evacuated by vomiting or by stool,
and death ensues through impediment to the circulation or respiration,
through the presence of abnormal quantities of certain substances, as
potassa salts, and phosphoric acid in the blood, or through various second-
ary (often inflammatory) affections.

2. INCREASE OF THE AMOUNT OF WATER IN THE BLOOD.

In disease, this condition occurs under all the conditions which bring
about a reduction of the total amount of blood, especially losses of blood
and albuminous substances (*vide* p. 519 and p. 526), as well as inanition
from whatever cause; it is produced, furthermore, by interference with the
excretion of water through the kidneys (even after experimental removal
of these organs, or ligature of the ureters), through the skin; perhaps also
in extensive burns. (In pregnancy?)

The phenomena and consequences of HYDRÆMIA are in part like those of
anæmia and of hypalbuminosis (*vide supra*); and often hydræmia is the
most important cause of so-called cachectic or hydræmic dropsy (*vide* p.
234). This dropsy makes its appearance often without other cause, at
times through the concurrent action of relatively slight mechanical cause
of the most various sort. Its mechanism consists in the not as yet fully
known physical and chemical laws which determine increased filtration
and diffusion of the water of the blood into the tissues.

BERNSTEIN (*Med. Centralbl.*, 1867, No. 1) observed after injections of fluid (water

or blood: in rabbits 25 C. cent., in dogs 45 C. cent.) a diminution in the number of arterial pulse-beats, persisting for a few minutes, and gradually passing to the normal. This reduction of pulse-rate produced by increased blood-pressure, took place through the vagi.

BECQUEREL and RODIER believe that dropsy (which they called symptomatic dropsy) must occur if there be 6% of albumen in the blood; though this occurs only with simultaneous increase of pressure. Dropsy may be produced by injecting an abundance of water into the vessels of an animal (DONDERS, KIERULF, L. HERMANN); but it quickly disappears because of increased urinary secretion, if the kidneys be healthy. We are not referring in this place to a mere artificial serous cachexia, for the force of the heart gradually diminishes, and accumulation of blood takes place in the veins, if blood be replaced by water. Abundant drinking does not conduce to dropsy.

That blood deficient in albumen escapes more easily from the vessels is shown by the following experiments (among others) of BRÜCKE. A frog, one of whose sciatic nerves was cut, placed in a large glass vessel upon a piece of moist filtering paper, showed, after a few weeks, œdema of the palsied leg. Upon the frog's being fed with meat-worms, the œdema quickly disappeared; returned in inanition; and disappeared again under the influence of food, etc.

VI. EXCESS OF FAT IN THE BLOOD.

An excessive proportion of fat in the blood may show itself under two entirely different circumstances.

Either, as a result of crushing, suppuration, disintegration, the fat of subcutaneous connective tissue, and (especially) of the marrow of bones, is taken up by lymphatic vessels or directly by bloodvessels, and produces embolism of the pulmonary capillaries, more seldom of the capillaries of other organs; these emboli being absorbed in an unknown manner without doing any mischief, or else producing local alterations, metastatic hyperæmia, inflammation, etc. (vide p. 200, p. 209, and PYÆMIA).

Or, the superfluous fat is derived from the food. We here only consider the fat thus derived, the so-called FATTY or CHYLOUS BLOOD-SERUM.

This is observed a few hours after a meal containing an abundance of fatty material, perhaps independently of this in habitual drinkers. The blood-serum may, in this way, become so milky, that it will show upon its surface a cream-like layer, containing innumerable small, and a few large oil-globules.

The consequences of habitual chylous blood are not thoroughly known. In many cases, with simultaneous sedentary habits, there arises fatty abdominal deposit. There occurs also, probably, a lessening of the absorption of oxygen by the blood-corpuscles. Under a regimen rich in hydro-carbons, and deficient in albumen, the so-called fatty degeneration of tissues (muscles, liver) may appear acutely. In such circumstances also fluid fat is sometimes found in the blood.

VII. CHANGES IN THE FIBRIN OF THE BLOOD.

Such changes are not yet known with certainty, because we have, until recently, been acquainted only with so-called coagulated fibrin, its insoluble

(in water) form, because separate study of fibrino-plastic substance and of fibrinogen was not yet possible; and because the statements concerning increase or decrease of fibrin in disease (so-called HYPERINOSIS and HYPINOSIS) were nearly all based upon increased rapidity of coagulation, and upon the firmer consistence of the clot derived from blood-letting.

[Consult: WILLIAMS, *Principles of Medicine*, Phila., 1857, p. 150. ANDRAL et GAVARRET, *Recherches sur les modifications de proportion de quelques principes du sang* (*fibrine, globules, etc.*) in *Ann. de chimie et de physique*, t. LXXV., Nov. 1840.—ED.]

HYPERINOSIS is said to be present in inflammatory diseases, especially those of the respiratory organs, of serous membranes, and of articulations; HYPINOSIS in scorbutus and analogous states.

Increased coagulability of fibrin in the living body, INOPEXIA, is said to be the cause of the formation of thrombi.

VIII. PLETHORA.

(POLYHÆMIA. REPLETION.)

PLETHORA is the name given to that condition in which the mass of the blood is absolutely increased, and in which its composition is not materially changed. But, as we do not know what the normal amount of blood is, the existence of true plethora cannot as yet be demonstrated.

The total mass of blood in the adult is at the present time considered to amount to $\frac{1}{12}$ to $\frac{1}{14}$ of the weight of the body: in the newly-born it is smaller, according to several observers, only $\frac{1}{19}$; in old age it gradually diminishes.

Compare the physiological researches (differing much) of ED. WEBER and LEHMANN, of WELCKER, BISCHOFF, PANUM, HEIDENHAIN, GSCHEIDLEN, BROZEIT, SUBBOTIN, RANKE, STEINBERG, and others. Fattened animals have a relatively smaller, starved animals a relatively larger amount of blood.

Many conditions designated as plethora are probably the following states:

POLYCYTHÆMIA (polycythæmia rubra), that is to say, an increase in the number of red corpuscles. Yet this condition cannot as yet be satisfactorily demonstrated, because the methods now used to enumerate the corpuscles are not sufficiently exact, and because the number of red globules probably varies a good deal in physiological conditions. Such a difference in numbers appears to have been demonstrated only with reference to the male and female sexes. Polyhæmia, and polycythæmia as well, are in most cases only transitory states.

PANUM (*Virchow's Archiv*, XXIX., p. 481) observed that the blood of young dogs was much richer in solid constituents than that of their mother. Comparisons of the solid residue, of the specific gravity, and of the coloring property of the whipped blood, showed, farther, that it was extraordinary richness in red corpuscles which distinguished the blood of the bitch from that of the puppies. This is in accordance with the results of DENIS and POGGIALE. Besides, PANUM found that the concentrated blood of the newly-born soon becomes poorer in solid ingredients (especially blood-globules), and richer in water and fibrin; and that later, after growth is complete, it again contains more solids, without, however, ever attaining the proportions present in the newly-born.

According to ANDRAL and GAVARRET, and DELAFOND (*Ann. de chimie et de physique*, 1842), the blood of the strongest animals on the average contains the largest propor-

tion of red globules. The number of blood-globules in the sheep being taken as a standard at 93, there was found in finer and stronger sheep an amount equal to 101–110, and in the strongest sheep of the drove 123. VIERORDT (*Archiv f. phys. Heilk.*, 1854, p. 409) found in a marmot during hibernation (in 1 C. cent of blood) 7,748,000 globules on November 1st; 5,100,000 on January 5th; and 2,335,000 on February 4th.

Polyhæmia, or especially polycythæmia, makes its appearance: in young individuals, and in the period of greatest development, especially if the persons have experienced a change from bad diet with much labor to better food and diminished exertion; when habitual hæmorrhages are suppressed (menstruation, nose-bleed, hæmorrhoidal flux, regular venesection); when the secretion of abundantly suppurating sores is arrested; sometimes after transfusion.

According to ANDRAL and GAVARRET, and others, the blood in the last months of pregnancy becomes poorer in red corpuscles and albumen, richer in white corpuscles, fibrin, and water. SPIEGELBERG and GSCHEIDLEN (*Archiv f. Gynäk.*, 1872, IV., p. 112) observed in bitches during the first half of pregnancy no increase in the amount of blood, a change which does take place soon after the middle period of pregnancy. In this increase the change in the amount of water is unimportant, it may even not occur; the amount of hæmoglobin diminishes within limits allowed by nutrition.

The ingestion of nutritious and abundant food, during an inactive life, seldom leads to the development of a plethoric condition, but usually conduces to corpulency. This luxurious living involves excess in all articles of food, or in a few. In the first case no attention is to be paid to the water and salts; as excessive quantities of these are at once excreted, water through the skin and kidneys, salts through the kidneys. With an abundant supply of nitrogenous and non-nitrogenous foods the body-weight increases, the fat especially increasing; a copious supply of nitrogenous food augments the excretion of urea extremely; the use of much fat or hydro-carbons diminishes it. If a superabundance of easily oxidized non-nitrogenous substances (fats, hydro-carbons) be taken, the amount of fat becomes greater. With respect to this it is yet doubtful whether the fatty deposit derives directly from the superfluous fat in the food, or whether it is formed, indirectly, from the carbo-hydrates on the one hand, and from albuminous bodies on the other. Fat is deposited if only so much food be taken that the albumen contained in it will not suffice to oxidize the ingested fat; or if, together with albumen and fat, so much carbo-hydrate reach the blood that it (being more easily burned) will protect the fat from oxidation. Fat may be formed out of albumen if a sufficient amount of carbo-hydrates be present in the blood in addition to the albumen. No fat is formed directly from carbo-hydrates. As a result of excessive ingestion of nitrogenous substances there occurs a decomposition of the non-nitrogenous (glycogen, sugar), and the nitrogenous compounds of the body. The latter products ultimately appear in the urine as urea, uric, and hippuric acids.

The majority of the questions which come up here for consideration belong to the domain of the pathology of nutrition. Those conditions which determine fattening are of physiological and agricultural interest (*vide* p. 400). In the last decade the subject of diminution of fat, the so-called BANTING CURE, has acquired importance in the eye of physicians. If we wish to bring about an increase of fat we must prevent an accumulation of the circulating albumen, that is to say, prevent an increase of the intermediate fluids of nutrition. In a fat body the albumen derived from food is much more easily changed to organ-albumen, than in a lean body, in which it goes to increase the amount of circulating albumen, and is shortly in greater part

destroyed. There is, conversely, more fat destroyed and more of the stored-up fat decomposed, if there be a large amount of circulating albumen, as, for example, during the eating of an abundance of meat. There is then next to no fat produced, and, on the contrary, that which was laid by is reduced (PETTENKOFER and VOIT, also VOIT, *Zeitschr. f. Biol.*, V., p. 79, p. 329, IX., p. 1).

The manifestations of polyhæmia should be : increased sense of strength, a red, full face (in the dark complexioned there is a turgid, tense skin without redness of the cheeks, bright red mucous membranes, full pulse, strong cardiac impulse, full veins. Such individuals are theoretically healthy, but they suffer severely from morbid manifestations. They frequently have congestion of the brain, palpitation of the heart, a sense of fulness in the chest, shortness of breath ; and all of these more severely if usual hæmorrhages are suppressed. It is not demonstrable that serious secondary results (cardiac hypertrophy, etc.) are produced by long-continued polyhæmia, or by its frequent return.

The symptoms of plethora are likewise seen in transfusion, if it be done too rapidly or with too large a quantity of blood. Even paralysis of the heart and death may result from over-filling and distention of the right heart (PANUM l. c., MITTLER, *Vers. üb. die Transfusion des Blutes, Wien. Sitzungsber.*, Nov., 1868). LUDWIG (oral communication) was able to inject into a dog double the amount of the blood in its body, without observing any important symptoms except a slight increase in blood-pressure. We have as yet no researches on the excretion of carbonic acid, nitrogen, etc., in this condition.

By the name of PLETHORA APOCOPTICA is meant the supposed increase of blood which occurs in consequence of the sudden removal of a large part of the body, as, for example, amputation of an extremity : the organism contains the same amount of blood as before the operation.

O. WEBER (*Handb.*, p. 585), who has attempted to solve the question of the existence of *plethora apocoptica* by measuring the blood-pressure, found that after amputation of a whole hind leg in a dog the blood-pressure in its carotid artery was diminished. The traumatic fever which follows the operation increases the waste so much that a true increase of the amount of blood does not occur.

IX. LEUCOCYTHÆMIA.

J. H. BENNETT, *Edinb. Med. and Surg. Journal*, Oct., 1845 ; *ibid.*, Jan. and April, 1851, XIII., p. 323.—VIRCHOW, *Froriep's Not.*, Nov., 1845, p. 780 ; *Med. Ctrlzeit.*, 1846, Nos. 34, 36 ; *Gesam. Abhdl.*, I., p. 149, p. 191 ; *Archiv*, 1847, I., p. 563, II., p. 587, V., p. 79.—J. H. BENNETT, *On Leucocythæmia*, 1852.—VOGEL, *Virchow's Archiv*, III., p. 570.—UHLE, *in idem.*, V., p. 376.—VIDAL, *Gaz. hebdom.*, 1856, Nos. 7–15.—THIERFELDER and UHLE, *Arch. f. Phys. Heilk.*, 1858, p. 441.—MOSLER, *Berlin. klin. Wochenschr.*, 1867 ; *Die Pathol. und Therapie d. Leukæmie*, 1872.—NEUMANN, *Arch. d. Heilk.*, 1869, XI., p. 1.—WALDEYER, *Virchow's Archiv*, LII., p. 3.

Consult also the literature of lymphatic new-formations, p. 459 ; and p. 439.

LEUCOCYTHÆMIA, or LEUKÆMIA, that is to say, increase of the white corpuscles of the blood with simultaneous diminution of red corpuscles, is a transitory and symptomatic, or a chronic and essential disease. In both forms, the affection does not simply consist in an increased formation of white corpuscles, but also in checked transformation of them into red corpuscles.

1. SYMPTOMATIC, usually transitory LEUCOCYTHÆMIA : the so-called LEUCOCYTOSIS. This form occurs in pregnancy, after large hæmorrhages (*vide*

p. 519), in many inflammations, in a few acute and chronic diseases (cholera, acute yellow atrophy of the liver, pyæmia, intestinal mykosis, tuberculosis, cancer, syphilis, intermittent fever). Its probable causes are in many cases found to be acute or chronic enlargement of the spleen, or of groups of lymphatic glands (as the bronchial glands in pneumonia). The number of white corpuscles, in proportion to that of the red, may be doubled, or even more increased. The results of this condition are unknown.

2. ESSENTIAL, IDIOPATHIC, or CHRONIC LEUCOCYTHÆMIA.

Its causes are almost wholly unknown.

Age, sex, and condition are without influence. In many cases a connection can be made out between leucocythæmia and intermittent fever, constitutional syphilis, etc.

The amount of blood is not diminished, or not in any important degree. In the most severe grades of the affection, the blood, even when examined in small quantities, is paler than normal, looking as if mixed with pus. Blood removed by bloodletting and whipped, shows a red substratum, and a yellowish-white, soft and unctuous clot. In the dead body, the coagula in the vessels are yellowish-red, or yellowish-green, soft, unctuous, more so in the splenic veins, right side of heart, and pulmonary artery. The degree of INCREASE OF WHITE CORPUSCLES is very variable : varying from one white corpuscle to ten or two red corpuscles. Sometimes the white corpuscles differ from those found in healthy persons only by being relatively large ; they contain one or several nuclei (splenic leucocythæmia) ; sometimes they are smaller, possess one relatively large nucleus, or in place of the cells there are free nuclei (lymphatic leucocythæmia). At the same time the red corpuscles are absolutely diminished in number. In a few cases, undoubted transitional forms between white and red corpuscles have been seen (*vide* p. 524).

WELCKER (*Zeitschr. f. rat. med.*, CXX., p. 305) has demonstrated the actual diminution of red corpuscles in two cases.

The SPECIFIC GRAVITY of the blood is lessened (from 1055 to 1040 and 1035) ; this in part because of increase of the specifically lighter white corpuscles, in part because of the greater amount of water and smaller quantity of albumen in the blood. The other ingredients of the blood show no marked variation from the normal quantity ; except that, in consequence of the diminished number of red corpuscles, the proportion of iron is reduced, though hardly one half in the most cases. In a number of well-studied cases the blood gave an acid reaction, and contained xanthin, and hypoxanthin (both bodies not being, as in health, reduced to uric acid by oxygen) ; it also contained uric, lactic, formic, acetic (probably butyric) acids, and glutin. In the blood of the dead there have been found at times, colorless, elongated, octohedral crystals, probably derived from an albuminoid body.

In a case of QUINCKE'S (*Virchow's Arch.*, 1872, LIV., p. 537) the hæmoglobin in 100 grm. of blood amounted to only 5.8, instead of about 14.4 (splenic leucocythæmia).

The source of increase of the colorless corpuscles is either in an hyper-

trophy of the cells or of the whole pulp of the spleen, producing a ten- or twenty-fold enlargement (and even more) of that organ,—the so-called SPLENIC LEUCOCYTHÆMIA; or, it is in a similar affection of the lymphatic glands in one or several regions, internally or externally (especially those of the axilla, groin, and neck: the mesenteric and lumbar glands),—the so-called LYMPHATIC LEUCOCYTHÆMIA; or, it may be in a peculiar disease of the marrow of bones, by which the small bloodvessels are almost obliterated, the marrow-tissue contains an immense number of white corpuscles,—the so-called MYELOGENIC LEUCOCYTHÆMIA; or, lastly, and perhaps most frequently, the origin of the white corpuscles is in an affection of parts anatomically analogous to those named above, as the tonsils, the follicles of the throat and intestines. In addition, there are often seen in various organs, though especially in the liver, small (microscopic, and rarely larger) granulations having the characters of lymphatic new-formations (*vide* p. 460). In the above-named organs there are found white corpuscles, transitional forms from them to red corpuscles, and the other abnormal constituents of blood, at the same time as in the blood, and even in relatively larger quantities than in that fluid.

The hypertrophies and new-formations which occur in this disease have been shown by histological investigation not to differ from those which occur without co-existent leucocythæmia, as, for example, in pseudo-leucocythæmia. It is, besides, unknown whether the cause of leucocythæmia consists in an arrest of the transformation of white corpuscles into red, or in an increased supply of white corpuscles from various organs, or whether both causes act together.

The phenomena of leucocythæmia are partly explicable by the enlargement of the spleen or lymphatic glands (a sense of weight and fulness in the abdomen, of pressure upon adjacent parts, especially the diaphragm, etc.); in part by the constitution of the blood. To the score of the latter must be reckoned: the symptoms of anæmia of the skin, visible mucous membranes, brain (due to diminution of red corpuscles); those of general bodily weakness and marasmus (also due to want of red corpuscles); shortness of breath upon exertion, without any anatomical alteration of the respiratory organs (caused by want of red corpuscles, and probably also by temporary plugging of pulmonary capillaries by white corpuscles); the appearance of non-oxidized products of metamorphosis in the blood and the fluids derived from it (hypoxanthin and xanthin, fluid fatty acids, lactic acid); the usual though not constant increase of uric acid and urates in the urine (in consequence of incomplete oxidation from dyspnœa, etc.); the relatively late dropsical phenomena (the blood becoming deficient in albumen only at an advanced period of the disease).

PETTENKOFER and VOIT (*Zeitschr. f. Biol.*, 1869, V., p. 319) have published an exact observation of tissue-metamorphosis in leucocythæmia. It was ascertained that with equal feeding there was no marked difference between the destruction of tissues in the healthy body and that in a leucocythæmic person. The following are the figures:

	Albumen.	Fat.	Carbo-hydrate.	CO_2 by lungs and skin.	Oxygen taken in.
Healthy person	120	83	344	249	832
Leucocythæmic person	99	98	335	265	790

With the exception of exhalation of CO_2, all the excretions of the leucocythæmic patient were greater during the night: a result of retarded digestion. That the quiet leucocythæmic person should take up (with similar diet) as much oxygen as a

healthy individual, with such a lack of red corpuscles, is a demonstration of the great power of accommodation possessed by the human body.

LIEBREICH (*D. Klinik*, 1861) was the first to describe a *retinitis leucocythæmica*, visible to the ophthalmoscope. Consult also BECKER, LEBER, ROTH, SÆMISCH, STELLWAG, *Diseases of the Eye*, N. Y., 1873, p. 168. According to SALKOWSKI (*Virchow's Archiv*, L., p. 174), the relative increase of uric acid is a constant symptom of splenic leucocythæmia, and does not depend upon coincident conditions. The dependence of this upon incomplete oxidation was first rendered doubtful by the experiments of SENATOR, NAUNYN, and RIESS. Undoubtedly abnormal intermediate forms in the final products of tissue-metamorphosis, not due to invasion of the blood by splenic products, have as yet been found neither in the blood nor in the urine. In normal urine, and in that of leucocythæmic persons, no hypoxanthin-like substance is met with.

There are, besides, a series of symptoms which are not yet capable of explanation. These are frequent, abundant perspiration, at times severe gastric and intestinal disorders (great constipation), frequent hæmorrhages from the nose and intestines (probably in consequence of stagnating capillary circulation), menstrual disorders. Fever is at first only intercurrent, later continuous, yet moderate : it occurs without demonstrable inflammatory complication.

The course of leucocythæmia is always very chronic ; it lasts from six months to several years.

The issue of leucocythæmia is invariably fatal. Death is brought about by loss of blood (most commonly from the nose), by dropsy, marasmus, or by an intercurrent affection.

PSEUDO-LEUCOCYTHÆMIA, splenic (or lymphatico-splenic) anæmia or cachexia, HODGKIN'S DISEASE, TROUSSEAU'S *Adénie*.

In all important respects this disease resembles leucocythæmia, with the exception that the multiplication of white corpuscles is wanting. It is probable that the red corpuscles are very much diminished in number. The anatomical and histological alterations are met with sometimes only in the spleen, sometimes only in the lymphatic glands of internal and external organs, sometimes in other organs alone or in conjunction with the spleen and lymphatic glands. They sometimes present the characters of a true hypertrophy, sometimes it is only the cellular elements of the cytogenous tissue which are much increased ; in other cases there is a deposit of small, indifferent round cells and nuclei in the affected organs (liver, kidneys, intestines, etc.), to such an extent that a sarcomatous appearance is produced. The cells and nuclei in these deposits are sometimes not changed, sometimes atrophied, so that the new-formation has the appearance of a scrofulous mass, or of caseous tubercle.

The symptoms are in general like those of leucocythæmia. The course of the disease is usually more rapid ; and it probably always ends fatally.

HODGKIN, *Med.-Chir. Trans.*, 1832, XVII., p. 68.—WILKS, *Guy's Hosp. Rep.*, 1856, XI., p. 56 ; *Trans. of Path. Soc. Lond.*, 1859, X., p. 259.—WUNDERLICH, *Arch. f. phys. Heilk.*, 1858, XVII., p. 123 ; *Arch. der Heilk.*, 1866, VII., p. 529.—VIRCHOW, *Die krankh. Geschwulste*, 1864–5, II., p. 619. [French edition, vol. III., p. 11 *et seq.*, 1871.]—MÜLLER, *Berlin. klin. Wochenschr.*, 1867, Nos. 42–4.—Isolated cases by CRUVEILHIER, ROKITANSKY, LAMBL, BILLROTH, COHNHEIM, EBERTH, the AUTHOR, and others.

TROUSSEAU, Clinique Médicale, III., p. 555, 2me ed. Paris, 1865.

X. MELANÆMIA.

MECKEL, *Zeitschr. f. Psych.*, 1847; *Deutsche Klinik*, 1850, No. 50.—VIRCHOW, *Archiv*, 1849, II., p. 594.—HESCHL, *Zeitschr. d. Wien. Aerzte*, 1850, VI., p. 7; *Oest. Zeitschr. f. pract. Heilk.*, 1862, Nos. 40, 42, 43.—PLANER, *Zeitschr. d. Wiener Acad.*, 1854, X.—FRERICHS, *Günsb. Zeitschr.*, 1855, VI. ; *Klinik der Leberkrank.*, 1858, I., p. 325.—W. MÜLLER, *Ueb. d. fein. Bau d. Milz*, 1865. There are older observations by STOLL, BRIGHT, ANNESLEY, and others.

MELANÆMIA is that condition of the blood in which that fluid contains PIGMENT-GRANULES derived from the vascular system of the spleen, which granules circulate for a while, are arrested in the smallest capillaries (brain, liver, kidneys, etc.) for a while or permanently, thus giving rise to a number of severe symptoms.

The PIGMENT is usually black, more rarely yellow or brown. The particles are of a size varying from that of the smallest molecules to that of red corpuscles, and larger ; and present a pseudo-crystalline outline. The pigment in its early existence does not offer as much resistance to the action of acids and alkalies as it does later. The greater number of pigment granules are free ; some are inclosed in white corpuscles, or in cells. The free granules sometimes exhibit a thin, clear, concentrically stratified margin. Besides, the red corpuscles are diminished, and the white corpuscles sometimes increased.

The pigment of melanæmia is ALTERED HÆMATIN. It is derived from hæmorrhages (of the common kind, or *per diapedesin*) which occur in the hyperæmic spleen of subjects having long-continued malarial intermittent fever (at first of a pure type, but later often continued) ; also occurring, according to several authorities, in the liver and the brain. In the spleen such extravasations of blood occur so frequently under nearly healthy conditions that the so-called blood-globule-holding cells have been looked upon as normal. In later stages of the affection the pigment is found in the intervascular tissue, which is by it rendered thicker, and colored black. The pigment enters the blood directly, or with white corpuscles whose substance it has penetrated, after deposition in the stroma of the spleen or without it ; producing, if there be much of it, a gray or grayish-black color in all vascular organs, the gray substance of the brain, the kidneys (their cortex especially), the lungs, skin, mucous membrane, lymphatic glands, etc. (and the spleen itself). In most of the above-named organs, with the exception of the spleen, it lies within the bloodvessels, seldom also in glandular and epithelial cells. Affected organs exhibit, besides the pigmentary deposit, almost no alterations ; sometimes there are small hæmorrhages in the brain ; sometimes there is a degree of induration, in the spleen and liver especially.

E. H. WEBER (*Verh. d. sächs. Ges. d. Wissen.*, 1850) was the first to describe the pigmented liver of amphibia and its periodical appearance. According to REMAK (*Müller's Archiv*, 1852), the pigmented liver of frogs is produced by want of food and exercise. Both these observers erroneously believed the condition to be due to deposit of pigment in the hepatic cells. W. MÜLLER demonstrated the frequent presence of cells containing hæmatoidin and melanin in the splenic pulp of several vertebrata.

The color of pigmented liver resides, according to EBERTH (*Virchow's Archiv*, 1867, XL., p. 305), for the most part in white corpuscles, and in lesser degree apparently in the endothelium of bloodvessels. The affected white corpuscles are derived from the spleen. The black color of these cells is produced most probably by a change in the pigmentation of the cell-contents, in the course of development of the blood, so that pigment particles to a certain extent replace the normal fibrin of the blood, and the white corpuscles instead of being transformed into yellow corpuscles, undergo

melanotic degeneration.　The more spindle-shaped pigmented bodies, as well as the round pigment-cells which are united in groups in the liver, are probably in greater part derived from the spleen.　According to HESCHL, the pigment is formed by a spontaneous escape of the red coloring matter of blood-corpuscles into the walls of bloodvessels, especially those of the brain and spinal cord; thence into the blood.

According to ARNSTEIN (*Tagebl. d. Nat.-Vers.*, 1872, p. 219), bone-marrow also contains an abundance of pigment in all cases of melanosis after intermittent fever; some of it being in the bloodvessels, the greater part in the tissue itself incorporated into the lymphoid and other larger cells.　The pigment is produced in the vascular channels by disintegration of the red globules, is quickly taken up by the white corpuscles, remains a while in the capillaries of the spleen, liver, and bone-marrow, being ultimately lodged in the tissues.　In favor of this view is the distribution of pigment after artificial introduction of granular coloring matter into the vascular system.

The symptoms of melanæmia are partly those of anæmia, especially those of reduced number of red corpuscles (pale skin and mucous membranes, emaciation, dyspnœa, dropsical manifestations, probably also hæmorrhages from the intestines and seldom from other parts); other and characteristic symptoms are the dark, gray, or grayish-brown color of the skin and visible mucous membranes, more especially the microscopic demonstrations of pigment in the blood and (probably) also in the urine.　Other symptoms are such as are due to the temporary or permanent stuffing of parts of organs by pigment masses (there are local or general disturbances in the brain in consequence of passive congestion or capillary hæmorrhages), such as comatose or typhous states, more rarely delirium, vertigo, severe headache, convulsions; in the kidneys, albuminuria, hæmaturia, or anuria; in the liver, passive congestion of the radicles of the portal vein with consequent diarrhœa, intestinal hæmorrhage, ascites.　Conditions similar or analogous to those above named are also met with in cases of malarial poisoning without melanæmia.

BASCH (*Oestr. Jahrb.*, 1873. 2. H.) described a mild case of melanæmia, in which flakes containing finely granular brown pigment were excreted with the urine.

The issue in severe cases of melanæmia is fatal.　Milder cases may be cured, but the mode of cure is unknown.

[Dr. Wm. A. Hammond has recently (Transactions of the American Neurological Association, first meeting, New York, June, 1875) published interesting observations tending to show that the pigment of melanæmia may produce retinal embolism demonstrable by the ophthalmoscope; he has also often punctured the spleen by means of a long and fine trochar, and found the blood removed in this way to be charged with pigment, and pigment-cells.—ED.]

The name PSEUDO-MELANÆMIA is given to the coloring of tissues and vessels in the neighborhood of gangrenous parts during life, and other parts after death, by sulphide of iron.　The pigment consists in large or small rounded masses, or scales.　Decomposition sets the iron free from its union with the organic substance, and it combines with the sulphide of hydrogen.

Compare J. VOGEL, *Path. Anat.*, 1845, p. 158.—GROHE, *Virchow's Archiv*, 1861, XX., p. 306; XXII., p. 437.

XI. ICTERUS: JAUNDICE.

(CHOLÆMIA.)

The literature of jaundice is extremely large.　The most important writings are cited in the special paragraphs, with especial reference to those which possess an experimental or chemico-pathological importance.　Comprehensive recent works are

those of FRERICHS, *klinik d. Leberkrankheiten*, 1858, I., p. 80 [Syd. Soc. Edition, 1860].—LEYDEN, *Beitr. z. Pathol. d. Icterus*, 1866. Consult also the literature of acute poisoning by phosphorus, p. 305.
[MURCHISON, *Clinical Lectures on Diseases of the Liver*, 1868.—*On Functional Derangements of the Liver*, London, 1874.—ED.]

ICTERUS is that condition which is produced by the re-absorption of BILE ALREADY FORMED IN THE LIVER, more seldom by a TRANSFORMATION OF THE COLORING MATTER OF THE BLOOD INTO BILE-PIGMENT within the vessels; by which almost all the fluids and solids of the body are tinged of a yellow color by the bile-pigment, and with which there are mild or severe general symptoms produced by the biliary acids or possibly other substances.

1. MECHANICAL OR HEPATOGENIC ICTERUS: ICTERUS OF ABSORPTION OR OBSTRUCTION.

Mechanical icterus is produced in the following way: the bile produced in hepatic cells is prevented from escaping into the smaller or larger biliary ducts, or into the duodenum, is placed under a higher pressure and passes into the blood- and lymph-vessels, and thus directly or indirectly colors nearly all the fluids and tissues of the body yellow. The evidence which supports the above explanation is derived partly from experiments (ligature of the *ductus choledochus*), and partly from clinical and pathologico-anatomical observations.

The causes of mechanical icterus, by narrowing or closure of the biliary passages consist either in diseases of parts adjacent to the bile-ducts (pressure of tumors in their immediate vicinity, in the duodenum, the head of the pancreas, in the hepatico-duodenal ligament, in the liver itself, in other parts of the abdominal cavity; or from constriction by cicatricial tissue in the above-named peritoneal fold, or near it, etc.); sometimes in disease of the biliary ducts themselves (spasm (?) and paralysis (?) of the ducts, gall-stones, catarrhal secretion and pus, catarrhal swelling, new-formations in the mucous membrane, etc.)

The various causes which prevent the expulsion of bile probably do not need to be very intense, since in the guinea-pig and most likely also in man the normal pressure under which bile escapes is very small (HEIDENHAIN, *Studien, u. s. w.*, 1863), and the movement of bile in the biliary passages is chiefly produced by the *vis a tergo* of the secretion (the smaller bile-ducts not possessing a muscular coat), and by the reduction in the size of the abdominal cavity produced by respiratory movements.
The mechanical production of icterus was first experimentally demonstrated by SAUNDERS (*Abh. üb. d. Structur, u. s. w., der Leber*, 1795); and verified by TIEDE-MANN and GMELIN, and many others.
SENATOR (*Berl. klin. Wochen.*, 1872, No. 51) has described four cases of so-called menstrual jaundice. They were periodical attacks of jaundice corresponding in time to abnormal menstruation (scanty or suppressed); and were dependent upon vicarious congestion of the liver or biliary passages.

To the category of mechanical jaundice also belong those cases in which in consequence of impeded movement of the right half of the diaphragm (diaphragmatic pleurisy, peri-hepatitis), or of diminution of the respiratory movements, the diaphragmatic movements necessary for the excretion of the bile fail.
Likewise of mechanical origin is that form of jaundice which is produced by disorder of the hepatic circulation, causing altered conditions of diffusion (diminished lateral pressure in the portal capillaries, and easier transfer of bile); so is that occurring after thrombosis of the trunk or large

branches of the portal vein, after stoppage of numerous interlobular veins by pigment, and after persistent hæmorrhage from radicles of the vena portæ. The icterus of the new-born is to be explained in the same way: it arises, if, immediately after birth, the portal vein receives no more blood from the umbilical veins.

The last-named form of icterus was first studied by FRERICHS. NAUNYN (*Arch. f. Anat., Phys., etc.*, 1869, p. 579) deduced from BERNARD'S and VOIT'S physiological icterus, observed in dogs especially in the fasting state (occurring in cats and man under similar conditions), that its production was owing to diminution of blood-pressure in the liver, such as must take place in the fasting state. For, since in this condition the afflux of blood to the intestinal canal is much less than during digestion, it follows that the lateral pressure in the portal vein and the hepatic capillaries must be less during abstinence. HEIDENHAIN had already shown the great dependence of active secretion of bile upon this pressure. The above-named jaundice is consequently a resorption-icterus, without the concurrence of obstruction to the flow of bile.

The disorders which are produced by mechanical jaundice depend partly upon the absence of bile in the intestines, partly upon the influx of bile into the vascular system.

In consequence of arrest of flow of bile into the intestines, the intestinal contents and fæces are wholly free from bile. They become gray or even white, clay-like if there be fat in the food, and solidify upon cooling of the fat; in other cases they preserve their normal color, or are only a little paler. Their forward movement is diminished because the water of the bile is wanting, and perhaps also because bile is a stimulant of intestinal peristaltic movements. From both these causes, and because bile hinders decomposition of the intestinal contents, flatulence and offensively smelling stools appear, especially if the diet be largely composed of animal matter. Whereas the digestion of nearly all substances appears to go on normally, the absorption of fat is diminished, seldom arrested; because the bile, especially the biliary acids, facilitate the passage of fats through capillary apertures (making the moist membranes penetrable by fat, and rendering possible the filtration of the fat through the membranes under slight pressure, and increasing the diffusion between fats and aqueous solutions). There is often a repugnance to eating fatty food. With this exception the appetite is often good, a little diminished, or even increased: in cases showing the first peculiarity emaciation is chiefly observed.

The whitish-gray, silvery color of the fæces in case of arrested flow of bile into the intestines depends wholly upon the fatty ingredients of the food, and when patients eat food free from fat their stools assume a natural aspect (F. HOFMANN). Compare the experimental researches of ARNOLD, *Zur Physiol. d. Galle*, 1854; of BIDDER and SCHMIDT, *Die Verdauungssäfte u. s. w.*, and others. The emaciation which is produced by the formation of a biliary fistula depends according to VOIT (*Zeitschr. f. Biol.*, 1869, V., p. 329) upon the fact that diminution or arrest of absorption of fat greatly increases the consumption of albumen; so much so that at last more meat is needed for the support of the animal than it can digest. Entrance of bile into the stomach precipitates the pepsin and prevents gastric digestion for a long time. (BURKART.)

The passage of bile from the biliary passages into the veins and lymphatics takes place a few hours after the occurrence of obstruction. After about twenty-four hours the blood shows a distinct yellow tinge; the urine after about forty-eight hours; the conjunctivæ and skin in two or three days.

It is probable that the blood takes up all the elements of the bile. Most easily demonstrable is the bile-pigment, which, especially bilirubin, gives the serum of the blood a distinct yellow color; this admixture first producing the yellow hue of the skin and mucous membranes, although later they are also colored by the biliary pigment which the tissues themselves contain. The biliary acids are present in the blood in much smaller quantity, and are much more difficult of demonstration. Most probably cholesterin also enters the blood; at least the proportion of this substance is increased. Beyond this, the blood shows nothing abnormal.

The BILIARY PIGMENT and the biliary acids exert very different effects upon the organs of the body. The bile-pigment contained in the blood goes with the serum from the capillaries into the tissues, and imparts to them a diffused yellow tinge. Later, there appear in the tissues yellowish, greenish, or brownish molecules, in some cases still later larger granules colored in the same way. The icteric hue is present in nearly all tissues, especially in the heart itself and the vascular walls, all epithelia (their nuclei are less stained as a rule), the bones and teeth, and even new-formations: in jaundice of long duration in pregnant women the fœtus is stained. The cartilages, the central and peripheral nervous systems become stained very late and very faintly, or often not at all. Nearly all normal and pathological fluids become yellow: besides the blood, the urine, sweat, milk, various transudates and exudates; the saliva, tears, and mucus are probably never colored. In the liver the icteric color appears first and most directly, that is to say independently of the blood; the central part of the acini is colored most early and most intensely. The color reaches its maximum intensity in this organ and in the kidneys. In icterus of long standing the bile is found thickened (inspissated) in the smaller bile-ducts, which are usually dilated.

In cases of severe jaundice, there are sometimes found in the liver irregular, glistening, ruby-red, crystalline bodies, which are made up of BILIRUBIN separated from the stagnating bile. (WYSS, *Virch. Arch.*, XXXV., p. 553.)

The stained tissues in cases of moderate accumulation of bile, and when the icterus has not lasted too long, exhibit nothing abnormal in structure, and perform their functions normally. In more severe and longer-continued cases, however (occasionally quite early), there occurs albuminous turbidity, and even minute fatty metamorphosis and decomposition; conditions most noticeable in the liver and kidneys. Arrest of the function of these organs and death follow.

MAYER (*Oest. med. Jahrb.*, 1872, p. 133) has experimentally investigated the alterations of the hepatic parenchyma, which follow prolonged closure of the ductus choledochus.

The EXCRETION OF BILE-PIGMENT from the blood and tissues takes place through the kidneys: directly out of the former, indirectly (after the pigment has re-entered the bloodvessels and lymphatics) from the latter. This excretion is early and simply demonstrable in (fresh) icteric urine; in doubtful cases the pigment can be made known by chemical processes. At first the urine appears of a saffron-yellow, then reddish-brown, and when there is much bile-pigment dark brown. Withal it is nearly always clear, only exhibiting a sediment in case of coincident fever. It is seldom that

particles of bile-pigment are visible to the microscope.   Occasionally icteric
urine contains a small amount of albumen (hæmoglobin).

Microscopical study of the kidneys shows that not only there are par-
ticles of biliary pigment in the epithelia of the uriniferous tubes, but that
the lumina of these ducts are filled up to a certain extent with this pig-
ment, and are even plugged.

FRERICHS and others found LEUCIN and TYROSIN in the icteric and albuminous
urine of some cases of acute atrophy of the liver.

In summer, when water is drank in large quantities, traces of bile-pigment are
occasionally observed in human urine, without noticeable symptoms.

In some cases of true icterus the urine is of a very dark color, without containing
any pigment which responds to GMELIN's test.   The nature of the color in these
cases is unknown.

A color of the urine very similar to that of jaundice, though not produced by bile-
pigment, appears after impeded respiration in primary (pneumonia) or secondary
(malformations of the heart) pulmonary disease ; after the ingestion of rhubarb and
santonin, after admixture of blood with the urine.

Besides what passes out through the kidneys, a small amount of bile-pig-
ment is excreted through the sweat-glands ; as is shown by microscopic
examination, and also by the yellow tinge of perspiration, and of the linen.

The BILIARY ACIDS which enter the blood simultaneously with the pig-
ment, act injuriously, directly, upon the blood, and indirectly upon the
nervous system.   It is not known how much of these substances is required
to produce ill effects ; it probably varies according to the mode of produc-
tion of the jaundice, to personal peculiarity, but especially according to
further changes in the acids, and to the rapidity of their elimination.

The effect of biliary acids in large amounts upon the blood consists in
dissolution of the red globules.

The effect of biliary acids upon the nervous and muscular systems is
shown especially by retardation of cardiac contractions and pulse-beats,
which, clinically known for a long time, is demonstrable by experiment.   A
reduction of the pulse to forty beats per minute (fever being absent) is
not rare.   The reduction is brought about by paresis of the cardiac muscle.
The lowering of temperature, which is well-shown by experiments, is
explicable in the same way.   The respiratory movements are notably
reduced in frequency.   The whole striated muscular system is more or less
paralyzed, as is clinically shown by languor, debility, easy production of
fatigue.   Even in slight degrees of intoxication the sensorium shows
apathy ; in more severe cases stupor and coma, occasionally convulsions,
psychical excitement, even mania.

Nearly all the above-named effects have been artificially reproduced by injections
of cholate of soda in the blood.   VON DUSCH (Unters. u. Exper. u. s. w., 1854) was
the first to show the ill effects of injections of bile and biliary acids in the blood, and
he (as well as HÜNEFELDT) discovered that these substances dissolved the blood-
corpuscles.   RÖHRIG and HUPPERT (Arch. d. Heilk., 1863, IV., p. 385 ; 1864, V., p.
236) were the first to demonstrate that the well-known slow pulse of jaundice is the
result of the action of biliary acids, and that this effect is not produced through the
nervi vagi.   They also discovered the lowering of temperature.   TRAUBE (Berlin.
klin. Wochenschr., 1864, Nos. 4 and 15) showed that this diminution was directly due
to weakness of the cardiac muscle, to the lowering of blood-pressure in the aortic
system ; and the influence upon respiration was referred by J. RANKE (Arch. f.
Anat., Phys. u. s. w., 1864, p. 320) to a depressed condition of the muscular system and
the ganglionic apparatus.   The opinion that these effects are produced by solution of
blood-corpuscles (LEYDEN) is not tenable, because of the smallness of the number so
destroyed.

According to most authors the majority of symptoms in severe acute cases of jaundice (so-called acute yellow atrophy of the liver, *icterus typhoides*), as well as those in cases of chronic jaundice (granular liver, etc.), are caused chiefly by the biliary acids.

The ultimate destination of the biliary acids is as yet unknown ; the greater part of that which is injected in the blood disappears within the body, and only a fractional part is excreted by the urine. The increased diuresis which is occasionally seen in jaundice, facilitates the expulsion of these substances.

The biliary acids, in jaundice by absorption, are never present in the urine in quantities large enough to give a reaction to PETTENKOFER's test.

The view of FRERICHS and STÄDELER, that the bile-acids are wholly decomposed in the circulation, and become transformed into bile-pigment, is contradicted by KUHNE, NEUKOMM, HUPPERT, and others. HOPPE has shown that icteric urine contains both the conjugate biliary acids (glyco-cholic and tauro-cholic). (*Med. Centralbl.*, 1863, No. 22.)

Some of the symptoms of jaundice are not yet susceptible of explanation : for example, itching of the skin, with which various eruptions are probably connected, the sleeplessness, the hypochondriacal disposition, the bitter taste, the yellow vision, (xanthopsia), the scorbutic manifestations, the severe head-symptoms, etc.

The severe cerebral symptoms which make their appearance in many cases of jaundice have great clinical importance because of their frequently fatal issue. This condition is denominated CHOLÆMIC INTOXICATION, or bilious dyscrasia (HORACZEK), or *icterus gravis* (appertaining to WUNDERLICH's theriodic constitutional diseases). These phenomena are looked upon by many, *e.g.* FRERICHS, as uræmic, though they are very different from such. According to TRAUBE (*Ges. Beiträge*, II., p. 815) the cholæmic attack has so to speak a psychical character ; the patient becomes maniacal, and after one or several such attacks coma sets in, and in this state death occurs. According to others, *e.g.* LEBERT (*Virch. Archiv*, VII., p. 343), psychical depression (without mania) and coma are much more often observed. K. MÜLLER (*Arch. f. exp. Path.*, 1873, I., p. 213) found that injections of glyco-cholate of soda, of taurin, of prepared gall, did not produce the above-named conditions in animals : taurin proved absolutely harmless. Contrarily, symptoms like those of cholæmia were produced (according to LEBERT's conception) if a mixture of cholesterin in glycerine and soap-water was injected into the blood of dogs. MÜLLER concludes that the cerebral symptoms in severe forms of icterus and many hepatic diseases, are produced by the accumulation of cholesterin in the blood : CHOLESTERÆMIA so-called. Consult also the earlier work of FLINT, JR., *Am. Journ. of the Med. Sci.*, 1862, XLIV., p. 305 ; *Exper. Researches on a New Excretory Function of the Liver*, N. Y., 1868.—HARLEY, *Jaundice, its Pathol.*, etc., Lond., 1863.—TINCELIN, *Des principes biliaires*, Strasb., 1869.—PAGÈS, *De la cholesterine et son accumulation dans l'économie*, Strasb., 1869.*

The course of mechanical icterus is very variable, in dependence upon its causes. The condition may last only a few hours, days, or weeks, or may be prolonged for months and years. The escape of bile may in these cases be wholly or partially cut off. Intermittent icterus, of an irregular (seldom regular) type has been observed.

The termination of this form of jaundice in cure or death depends in part upon its causes, in part upon unknown circumstances. Death ensues through the diseases which cause the obstruction (carcinoma, etc.), or through bursting or perforation of the biliary passages, or through the

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* The credit of defining the morbid state CHOLESTERÆMIA belongs to AUSTIN FLINT, JR., although MÜLLER is placed first *supra*. The same unjust inversion was found in the literature of leucocythæmia (p. 545), and corrected, the editor taking the liberty of placing J. H. BENNETT's work at the head of the list. Consult also MURCHISON, *Functional Derangements of the Liver*, Lond., 1874.—[ED.]

overfilling of organs with bile-pigment, or through the action of the biliary acids upon the blood, etc.

2. CHEMICAL OR HÆMATOGENIC ICTERUS: BLOOD-ICTERUS.

HÆMATOGENIC ICTERUS arises by the transformation of the blood-pigment of destroyed blood-corpuscles into bile-pigment, in the circulation; which newly formed bile-pigment produces the same yellow tinge in various tissues, just as in mechanical icterus.

The causes of hæmatogenic icterus are not at the present as clearly demonstrable as those of mechanical jaundice. Icterus appears after injections of a large amount of water, of various acids (phosphoric, cholalic acid, etc.) in the blood, dissolving large numbers of red blood-corpuscles; seldom after inhalation of ether and chloroform. Clinical observation shows what is probably the same genesis, in intoxications, after snake-bite, in yellow fever, in a number of diseases in which jaundice not rarely shows itself (pyæmia, typhoid fever, chlorosis, inflammation of the lungs, malformation of the heart), in *icterus neo-natorum*, in the jaundice of emotion.

FRERICHS formerly thought that hæmatogenic icterus was produced by diminished transformation of biliary acids into biliary pigment in the blood. The occurrence of a kind of icterus without the participation of the liver, long ago observed, has been in recent times made the object of exact researches; BRESCHET (*Ephém. méd.*, 1826), VIRCHOW (*Verhandl. d. Ges. f. Geburtsh. in Berlin*, 1847; *Archiv*, I., p. 379), ZENKER and FUNKE, VALENTINER (*Zeitschr. f. klin. Med.*, *Neue Folge*, I., p. 46), BRÜCKE (*Wien. Sitzsber.*, XXV.), KÜHNE (*Virchow's Archiv*, XIV., p. 32), JAFFE (*Virchow's Archiv*, XXIII.), MUNK and LEYDEN (*Die acut. Phosphorvergiftung*, 1865). More recently it has, however, been asserted on good grounds that bilirubin and hæmatoidin are not identical (*vide* p. 313); consequently blood-icterus is not necessarily dependent upon bile-pigment. If the pigment of blood-icterus be derived from blood-pigment, this need not be bilirubin, but may be hæmatoidin (bodies of similar color, but of dissimilar composition).

NAUNYN (*Arch. f. Anat.*, etc., 1868, p. 401) has recently proved the statement that with the presence of free blood-pigment in the plasma, bile-pigment makes its appearance in the urine. In this way KÜHNE has explained the occurrence of bile-pigment in the urine after injections of salts of the biliary acids (FRERICHS), and after injections of water (HERMANN). Solution of hæmoglobin injected under the skin of dogs makes the urine contain hæmoglobin, but it is at first devoid of bile-pigment. Equally ineffectual were injections of blood whose corpuscles had been dissolved by repeated freezing. NAUNYN explains the difference between his results and KÜHNE'S by claiming that K. has not taken note of the frequent normal presence of bile-pigment in dog's urine. N. also frequently found biliary acids in the normal urine of man and dogs, and attributes the presence of both bodies in the urine to their absorption from the intestinal canal. That this does occur he showed by experiments consisting in feeding with biliary salts, and injections of bile-pigment in the small intestines, after which biliary acids and bile-pigment as well were demonstrable in the urine. The doctrine of hæmatogenic icterus lacks a basis upon facts, and the single means proposed for its distinction from icterus by absorption, viz.: the absence of biliary acids in the urine in the former kind (LEYDEN), is according to N. unreliable, as he has repeatedly found biliary acids in cases of so-called hæmatogenic icterus: that of pyæmia. The same author states that the inhalation of ether in large quantities will in some rare cases be followed by the appearance of bile-pigment in the urine; and he furthermore found injections of lac-colored blood, or of ether, into the small intestines, invariably caused the urine to contain bile-pigment, and he concludes from this that if the portal vein carries free hæmoglobin into the liver, this substance is transformed into bile-pigment.

VOGEL has also expressed himself against the existence of hæmatogenic icterus. According to V. and DRAGENDORFF traces of biliary acids are present in all urines, and yield, after proper preparation of the urine, PETTENKOFER'S reaction. This

destroys the principal argument in favor of the occurrence of a blood-icterus, the absence of biliary acids from the urine. (*Verh. d. Naturf.*, 1872, p. 75.)*

The consequences of blood-icterus are with respect to the saturation of tissues by bile-pigment, just the same as those of mechanical icterus. The liver is not, however, chiefly jaundiced; it is so only just as are the other organs. The biliary passages are empty, or slightly filled; and after death an obstruction to the flow of bile is never found. Usually the yellow color of the skin and mucous membranes exceeds that of the urine, because the pigment is rapidly excreted by the kidneys. The intestinal contents appear colored as usual, or a little less with bile. In blood-icterus the biliary acids are absent from both the blood and the the urine.

The most severe symptoms of this form of jaundice are in part due to the primary disease, in part to imperfect nutrition, and in part to direct alterations of nutrition (frequent fatty degeneration of the heart-muscle, liver, kidneys, etc.). The consequences of solution of blood-corpuscles have been over-estimated. In addition to the yellow color, the most striking symptoms are general weakness, feeble cardiac contractions, small pulse, albuminuria, tendency to hæmorrhage, etc. Itching of the skin is wanting.

In some cases the mode of origin of the jaundice cannot now be stated with certainty: as in chronic alcoholism, diseases of the heart, pneumonia, phosphorus-poisoning. In the majority of these cases the jaundice is probably of mechanical origin, produced by an acute catarrhal state of the duodenum, not surely recognized during the patient's life, and difficult of demonstration in the dead body. This catarrh especially affects the intestinal extremity of the *ductus choleduchus*.

In the last few years the mode of production of jaundice in poisoning by phosphorus has been much discussed. Whereas many (WYSS, EBSTEIN, BUHL) consider it as the consequence of a catarrh of the smaller biliary ducts, or as the result of their choking with degenerated (fatty) epithelium, or (MANNKOPF) as a result of hypertrophy of the hepatic cells, others look upon it (with hardly sufficient grounds) as hæmatogenic. In the more severe degrees of poisoning the urine contains bile-pigment and the bile-acids (WYSS and SCHULTZEN).

The opinion that many cases of icterus are caused by an accumulation in the blood of already formed biliary substances, so-called JAUNDICE BY SUPPRESSION, is no longer tenable in view of our present knowledge of the mode of production of the bile, and from the experiments of removal of the liver by J. MÜLLER, KUNDE, and MOLESCHOTT and others.

XII. SUFFOCATION.

The literature of suffocation is contained, so far as it is of general pathological interest, in the works upon general and special pathology, but in both is only treated very superficially. Its physiological literature is to be found in the same places. Literature on suffocation is voluminous, where it is of medico-legal importance, but here also its contents are meagre. The treatises on poisoning by carbonic oxide are but of limited interest to us.

SUFFOCATION is that change of the blood, whereby it becomes, in consequence of diverse alterations of the organs of respiration, circulation, etc., abnormally poor in oxygen, while the quantity of carbonic acid is diminished, normal, or, most frequently, increased.

The most marked symptoms of suffocation are cyanosis, dyspnœa, as also

* ICTERUS OF HÆMATIC ORIGIN, occurring in various traumatic states; consult A. PONCET, *De l'ictère hématique traumatique*, Paris, 1874.—[ED.]

certain phenomena on the part of the nervous system, heart, vessels, muscles, and secretions.

Suffocation occurs in different degrees. It appears either suddenly or gradually.

The highest degrees of suffocation, which rapidly end in death, have been examined more particularly in their physiological and medico-legal connection, while the lower forms, which are of longer duration and often occur paroxysmally, have attracted heretofore almost solely practical medical interest, but are still very little known in their general pathological aspect.

The CAUSES of suffocation are :

1. DIMINUTION OF, OR COMPLETE OBSTRUCTION TO THE PASSAGE OF AIR (oxygen) to the lungs. The circumstances which induce this are variable: breathing in a space devoid of air, or in an inclosed air-space; suffocation, strangulation, drowning, compression of the chest and abdomen, etc., by external violence; constriction or closure of the oral and nasal orifices, of the larynx, trachea, of the large, or many small bronchi by foreign bodies, which are introduced from without or originate within the body (blood, serum, pus, etc., which come there—substances which are produced in those parts, as mucus, pus, new-formations), by pressure from without (goitre, etc.) ; enlargements of the mucous membrane from œdema, exudations, new-formations, etc. ; diminution of the respiratory area of the lungs by blood, transudations, exudations, and new-formations within them (intense hyperæmia, hæmorrhage, acute and chronic œdema of the lungs, inflammation, syphilitic infiltration, tuberculosis, etc.), by diseases of one or of both pleural sacs (hydro-, pneumo-, etc., thorax), by enlargement of the heart, by voluminous new-formations from the bones, mediastina, by the diaphragm being placed too high ; pressure on the brain from diverse causes ; decrease or cessation of the respiratory movements from different diseases of the respiratory centre (injuries, hæmorrhages, etc.) in the medulla oblongata, *nn. vagi, phrenici, intercostales* (section of the same, especially of the first in young animals), etc. Impossibility of respiration from nervous influences : so-called *asthma acutum* or *laryngismus stridulus*, or pseudo-croup (?), real laryngo-spasm, *asthma bronchiale*, spasm of the diaphragm, constriction of the glottis in whooping-cough (?), hysteria ; diseases of the muscles of respiration ; difficult breathing on account of pain in the respiratory organs or in their vicinity, etc.

According to FODÉRA, A. COOPER, MALGAIGNE, BUDGE and others, the rapidity of respiration is very materially diminished, even to complete cessation, by pressure upon the brain. Both inspiration and expiration become less frequent and more prolonged (*Vide* p. 169.)

Stagnation of the blood in the vessels of the med. oblongata, as it occurs after ligation of the large arteries of the neck and after an interference with the efflux of the blood from the large veins of the neck, whereby the blood becomes poorer in oxygen and richer in carbonic acid, also produces dyspnœa. (*Vide* p. 170.)

Humpbacked people usually only show signs of dyspnœa, etc., after puberty, because, while the rest of the body grows normally, the development of the thorax is retarded.

Inhalation of air strongly impregnated with carbonic acid acts just like an obstruction to the introduction of oxygen to the lungs ; for as soon as the quantity of carbonic acid in the respired air equals that which is contained in the bronchi, the interchange of gases (which takes place, as is well known, according to the laws of diffusion) ceases.

Especially noticeable, physiologically, are curare, which paralyzes the respiratory muscles as well as other voluntary muscles, and strychnia, which produces tetanus in them. S. MAYER (*Oestr. Jahrb.*, 1872, p. 111) has called attention to the similarity

between suffocation and poisoning by strychnia : considerable increase in the force of the blood through irritation of the vaso-motor centre, diminution in the frequency of the pulse through central excitement of the vagus, spasms of the striped muscular fibres.

Another form of this class is produced by inhalation of gases not directly injurious, but which act by opposing the entrance of oxygen.

The so-called irrespirable gases, which produce spasm of the glottis, are carbonic acid, hydrochloric acid, sulphuric acid, nitrous oxide gas, ammonia, chlorine gas. (For further information, *vide* pp. 65–66.)

2. DECREASE OR CESSATION OF THE CIRCULATION OF THE (FUNCTIONAL) BLOOD of the lungs : closure of the pulmonary artery or its large branches by external pressure or strain, from thrombosis or embolism, from great debility of the right ventricle; obstructed efflux of the blood from the lungs into the left heart from different diseases, especially of the left ventricle ; in the fœtus, premature separation of the placenta or closure of the umbilical arteries ; obstructed blood-circulation on account of thickened blood, as in cholera, or on account of intermixture of foreign bodies (air- and fat-embolism). Furthermore, the direct transition of venous blood from the right to the left heart, through abnormal communication between the two, belongs to this category ; interruption of perspiration, for example, from varnishing the skin.

Oftentimes, combinations of the circumstances mentioned in 1 and 2 exist. To this class belong especially some unexpectedly occurring attacks of incomplete or complete suffocation in the course of chronic diseases ; *e.g.*, pleuritic exudations, phthisis pulmonalis, chronic cardiac diseases. In these cases the immediate cause of suffocation can neither be discovered during life nor after death.

Much more frequently than the higher degrees of suffocation do the lower ones come under the physician's observation. Their causes are in the main the same, only of slighter degree : especially the above-mentioned disorders of the air-passages, the lungs, and several diseases of the heart (most valvular diseases, diminished force of the heart from different causes). Many of these conditions only act when bodily motions or exertions, psychical excitement, changes in the blood, etc., are added. Or in a person suffering permanent dyspnœa, attacks of intense difficulty of breathing occur without any known cause, which often resemble, almost perfectly, experimentally produced suffocation : as in whooping-cough, spasmodic constriction of the glottis, in so-called bronchial asthma, in spasm of the diaphragm.

For the so-called CHEYNE-STOKES' phenomenon of respiration, *vide* p. 522.

3. EXPULSION OF THE OXYGEN FROM THE BLOOD through the agency of different substances, most frequently by displacement (carbonic oxide, rarely nitrous oxide), much more rarely by its rapid consumption (sulphuretted hydrogen, sulphuretted sulphide of ammonium).

Of these cases of poisoning the most numerous are by so-called coal-gas, that is a mixture of carbonic oxide, carbonic acid, carburetted hydrogen, etc., and those by illuminating gas, which contains also marsh gas and hydrogen. Poisoning by coal-gas is produced when to the burning coal not enough air is furnished to form carbonic acid. The oxygen is displaced from the blood by an equal volume of carbonic oxide and cannot re-enter the blood-corpuscles. The carbonic oxide can again be displaced by an equal volume of nitrous oxide. The latter first takes oxygen from the blood,

and forms hyponitric acid ; if more is introduced it even combines with the hæmo-globin.

By the action of alcohol, perhaps also by strychnia and morphia, the red blood-corpuscles' power of absorbing oxygen is reduced. According to DUJARDIN and DIDIOT (*Compt. rend.*, XXIII., p. 227) the red blood-corpuscles lose in some severe cases of typhoid fever, pyæmia, etc., their power of absorbing oxygen (?).

Anæmia also, whatever its cause may be, occasions, on account of the decrease of the red blood-corpuscles (the vehicles for oxygen), perhaps only on account of the diminished force of the blood, difficulty of breathing, etc.

The phenomena of suffocation can probably all be ascribed to the action of the blood of suffocation. Still the special explanation of the symptoms, especially of the lower degrees of suffocation, is difficult or impossible, because no experimental examinations exist in regard to them, and because in those single cases occurring in the observation of a physician compli-cations oftentimes exist whereby the already large number of physiological complications become more difficult to disentangle.

Furthermore, the diverse phenomena from the same or almost the same cause are different according to the individual : this does not only appear in the common pathological cases, but especially in cases of poisoning : we sometimes see cases of the same intoxication, for instance from coal gas, wherefrom the one slightly sickens, the other not, and the third dies.

The popularly received idea which existed for a long time, that in some cases of suffocation certain specific appearances are present, as well in life as after death, as in the death from strangulation, drowning, etc., has not been corroborated. This is the case only with the poisons.

The blood is in the higher degrees of suffocation of a dark blackish-red color (excepting from poisoning by carbonic oxide and illuminating gas, when it is a light red) ; furthermore, it is still fluid in the corpse, or at least coagulates slowly or incompletely. The difference between venous and arterial blood has disappeared. The blood no longer contains separable oxygen (the hæmoglobin shows one absorption band in the green). The carbonic acid is usually increased, but on the whole does not exceed very much that contained in normal venous blood ; the blood contains consider-able free carbonic acid ; the carbonic acid and nitrogen in their combina-tions show no marked change in quantity. Most likely there is formed within the blood through the suffocation one or more substances which in normal conditions become rapidly more highly oxidized, but which cannot be consumed when the oxygen is in insufficient quantity.

In the lesser degrees of suffocation, which develop gradually in days, weeks, etc., the blood is only slightly darkened ; a distinct difference still exists between arterial and venous blood.

The dark color of the blood of suffocation (and of the corpse generally) is due to the decrease or entire absence of oxygen, not to the larger quantity of carbonic acid. Arterial blood, through which a stream of carbonic acid is passed, very soon darkens, but only because carbonic acid, like nitrogen and hydrogen, expels the oxygen.

Normal blood contains about 18 vol. $\%$ O, 1 to 2 vol. $\%$ N, 25 to 42 vol. $\%$ CO_2. But the actual quantity of oxygen is not only different in arterial and venous blood, but also in the several kinds of veins : it is dependent upon the number of blood-corpus-cles, upon the rapidity of the circulation, the force of the blood, the functional activity of the organs, etc. The oxygen of the blood is mostly chemically combined with the hæmoglobin of the blood-corpuscles ; a small quantity is absorbed by the serum. The carbonic acid belongs mainly to the serum : partly it is chemically com-

bined (only to be expelled by acids); partly it is only absorbed or loosely chemically combined (with carbonate or phosphate of sodium). The blood-corpuscles contain carbonic acid in changeable (usually small) amounts.

In 100 vols. they are:

in inspired atmosph. air : 20.8 O, − 79.1 N, − 0.04 CO_2 ;
in expired air : 16.0 O, − 79.5 N, − 4.4 CO_2 ;
in the air of suffocation, *e.g.* in closure of the trachea : 11 − 5 O, − 79.5 N, − 9 − 15 CO_2.

The blood of suffocation contains in 100 parts (in dogs), from the time when reflex irritability had ceased in the cornea (A. Schmidt): no O, − 1.3 − 8 N, − 33.3 − 43.9 CO_2.

According to Setschenow (*Wien. ac. Sitzgsber.*, 1859, XXXVI., p. 293), the oxygen does not disappear from the blood and from the air contained in the lungs of strangulated dogs in proportion as the carbonic acid increases. While 100 vols. of blood of healthy dogs contain 49.4 and 48.2 vols. of gas, they only contained in strangulated animals 45.4 and 32.6, etc. : the whole quantity of gas was therefore decreased at the expense of the oxygen.

The increased desire to breathe, difficulty of breathing, DYSPNŒA, is the most marked symptom of suffocation. It appears in two different forms: either not increased, even slower, but deeper,—or rapidly repeated, but superficial respirations. Sometimes it is continuous, sometimes absent or only slight during repose, to appear again during exertion, or, in consequence of unknown circumstances, even reaching a high degree. Occasionally it is regularly intermittent (some cases of hysterical dyspnœa, etc.). The largest number of respiratory movements is found in those cases mentioned in 1, especially if the respiratory area diminish rapidly and breathing be at the same time painful, as in hysterical people.

The cause of dyspnœa is the insufficiency of free oxygen for the nervous centre of respiration, to which is usually added an increase of carbonic acid. Experimentally it is shown that want of oxygen or superfluous carbonic acid in the blood, or both these conditions combined, increase the number and force of inspirations and expirations, and the number of muscles which are called into action. A very great insufficiency of oxygen destroys the excitability of the respiratory centre : asphyxia is produced.

The more immediate relations of dyspnœa, the actions of the different respiratory muscles, the relation of inspiration to expiration, etc., cannot be discussed here. The increased or prolonged respiratory movements in many cases compensate the disturbance.

If the number of respirations be voluntarily increased, that is above the quantity necessary for the body, while their depth remains nearly normal and even, the absolute quantities of carbonic acid increases, but not in proportion to the increase of the number of respiratory movements, because the percentage of carbonic acid in the expired air diminishes. (Vierordt.) If the depth of the respirations be increased, while their duration remains normal, the absolute quantities of carbonic acid increase, but not in proportion as the depth of the respiration-increase, because the percentage of carbonic acid in the expired air diminishes. (Vierordt.) The more frequent and at the same time deeper respiratory movements which accompany active muscular exertion, therefore, increase the excretion of carbonic acid considerably.

Leichtenstern (*Z. f. Biol.*, VII., p. 197) made experiments in regard to the volume of the expired air under different circumstances. Just like Rosenthal, he found no diminution in the volume of expired air after section of both vagi. After production of pneumothorax on one side the volume of expired air sinks to about half of the former quantity of both lungs. After constriction of the air-passages, as is well known, the number of respirations decreases, but their depth increases ; the volume of expired air sinks considerably. Morphia decreases the volume, as also section of the spinal

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cord, cooling the animal and varnishing the skin. Heating, on the contrary, increases the volume of expired air.

The CAUSES of dyspnœa have been the subject of a series of experiments, which already are in a measure of direct pathological interest.

W. MÜLLER allowed the animal to inhale a mixture of N and O. When the quantity of oxygen attained 15.4 per cent. (instead of as normal 21.0), the respiration became deeper and more prolonged ; no noticeable accidents occurred. At 14.8 per cent. the animal breathed for twelve minutes without marked difficulty. At 7.5 per cent. it breathed fifteen minutes, the respirations were deeper and more prolonged, as in slight dyspnœa. At 4.5 per cent. it breathed for fifteen minutes very strongly and in a prolonged way, with exertion of all muscles. At 2.9 per cent. great restlessness occurred after thirty seconds ; after thirty seconds more severe symptoms of suffocation. More rapidly yet did these appear at 1.7 per cent. According to MÜLLER, the carbonic acid in the atmosphere has no influence on the respiratory movements ; only the diminution of oxygen produces dyspnœa.

TRAUBE (*Med. Centralz.*, 1862, No. 38 and 39 ; *Ueber Wesen etc. der Erstickungserscheinungen*, 1857) proved against MÜLLER : 1, that carbonic acid acts as an intense excitant upon the respiratory nervous system ; 2, that it strongly and directly excites the terminations of the vagus which are contained within the lung ; 3, but that it does not produce difficulty of breathing in that way. For if TRAUBE introduced into an animal, in whom he had produced apnœa, a mixture of gas which contained more oxygen than atmospheric air, and at the same time considerable quantities of carbonic acid, respirations shortly after appeared and soon also dyspnœaic symptoms. This was also the case when the vagi of the animal were severed in the neck : but the dyspnœa was considerably stronger than when the vagi were intact. Further experiments with indifferent gases showed that if they were introduced unmixed into the lungs (hydrogen, nitrous oxide) respiratory movements and dyspnœa began. From this TR. concludes that there is a dyspnœa from oxygen and one from carbonic acid. The symptoms which precede suffocation are occasioned by diminution of the introduction of oxygen and by obstruction to the exit of carbonic acid.

According to THIRY (*Rec. des trav. de la soc. all. de Paris*, 1865), not only the evaporation of the carbonic acid which is dissolved in the serum of the blood is diminished through an interruption in the interchange of gases in the lungs, but the decomposition of the substances containing the carbonic acid chemically combined also proceeds more slowly : the blood becomes richer in free and in chemically combined carbonic acid. If the carbonic acid in both conditions acts as an irritant on the respiratory nervous centre, then indifferent gases, which are introduced into the blood in place of atmospheric air, must induce dyspnœa, as a direct obstruction to the interchange of the gases in the lungs. For though by such a gas the diffusion of the free carbonic acid can be produced just as completely as by atmospheric air, the substance containing the chemically combined carbonic acid remains undecomposed. The blood becomes here also richer in carbonic acid, and therefore dyspnœa is produced. Accordingly the dyspnœa from oxygen would only be a dyspnœa from carbonic acid. The diminished introduction of oxygen would produce dyspnœa, because, in consequence of the insufficient introduction of oxygen, the blood remains richer in carbonic acid than normally. And an obstruction to respiration would only cause dyspnœa, because the quantity of free and combined carbonic acid increases in the blood.

According to DOHMEN (*Unters. aus d. phys. Labor. zu Bonn*, 1865, p. 83) the inhalation of pure carbonic acid causes the volume of expired air and the depth of the respirations to increase considerably, their frequency only slightly, within one and a half minutes before death. In breathing a mixture of carbonic acid and oxygen, which contained more oxygen than atmospheric air, the volume of the expired air and the depth of the respirations increased to double the normal amount ; later on they fell below the normal standard, but the animal remained alive for a long time. As the animal received hereby always enough oxygen, the increase at first as well as the later decrease must be in consequence of the carbonic acid. Therefore insufficiency of oxygen, as well as carbonic acid, acts excitingly upon the respiratory centre, and accumulation of carbonic acid acts paralyzingly upon the nervous system.

According to PFLÜGER (*Arch. f. d. ges. Phys.*, 1868, I., p. 61), the carbonic acid may be increased, diminished, and even remain unchanged during breathing of indifferent gases. The most intense dyspnœa can be produced while the carbonic acid in the body is not increased, and even while it is considerably diminished. If therefore the gases in the blood have an influence on the medulla oblongata, the always existing insufficiency of oxygen only can be the cause of the fulminating phenomena of dyspnœa and asphyxia. The cause of dyspnœa must be ascribed to the insufficiency of free oxygen in the tissues of our bodies, for example the medulla oblongata. Because

readily oxidizable substances are constantly formed in the body and the blood through the animal tissue-changes, an increase and an abnormally large accumulation of these products must appear when there is a want of oxygen. These readily oxidizable substances are, according to A. SCHMIDT, the generators of dyspnœa. No known poison kills with phenomena similar to those fulminating symptoms which appear from closure of the trachea, excepting hydrocyanic acid. The latter poisons by suffocation, caused in the first instance by a serious alteration in the mechanical actions of respiration, and partly secondarily, partly primarily, by paralysis of the heart. But the animal not only breathes to receive oxygen, but also to expel carbonic acid. From experiments by PFLÜGER it follows that insufficiency of oxygen produces dyspnœa, but that carbonic acid in large accumulations does the same or acts similarly. But the accumulation of immense amounts of carbonic acid in the blood can be much longer sustained than the insufficiency of oxygen, which kills in the most rapid way with fulminating phenomena of suffocation. Abnormally large accumulations of carbonic acid, it is true, also gradually act fatally, but with symptoms which, if a sufficient amount of oxygen be present, can never be compared to the violent and rapid action caused by insufficiency of oxygen. Nevertheless, carbonic acid has an exciting action upon the medulla oblongata. DOHMEN saw an enormous increase in the depth and frequency of the respirations, with ten per cent. of carbonic acid and ninety per cent. of oxygen in the respired gas. It must be acknowledged, therefore, that even a small quantity of carbonic acid in the blood causes excitation of the medulla oblongata.

NASSE (*Med. Ctrlbl.*, 1870, No. 18) believes with BROWN-SÉQUARD that those products of nutrition which are not excreted, especially carbonic acid, are the causes of the respiratory movements, as well as of dyspnœa, *vide supra.*

The other symptoms of suffocation are ascribed sometimes to insufficiency of oxygen, sometimes to superabundance of carbonic acid in the blood. Both cause an intense irritation of the brain and medulla oblongata.

On the part of the CENTRAL NERVOUS SYSTEM we find in the higher degrees of suffocation (besides the above discussed irritation of the vagus and the consequent increased rapidity of respiration) general clonic spasms, similar to epileptic ones. They originate most likely in consequence of the poverty of oxygen in the blood, perhaps also through anæmia, which is a consequence of the constriction of all small arteries of the body, therefore also of the cerebral arteries, through an increased quantity of carbonic acid in the blood.

The reflex activity of ganglion-cells is greatly influenced by the quantity of oxygen present in the blood, so that with the increased quantity of oxygen, reflex activity in apnœa is diminished or ceases altogether. Therefore it is generally accepted that the spasms are due to insufficiency of oxygen in the blood, being explained in the same manner as those which appear after hæmorrhage or ligation of the four large cerebral arteries (see p. 169). The fact that they cannot be produced by introduction of mixtures of gas containing much carbonic acid as well as oxygen into the lungs, corroborates this. Others, for instance BROWN-SÉQUARD, lately also O. NASSE, ascribe them directly to the abundance of carbonic acid in the blood, which many dispute. Lastly, it is questionable whether the spasms originate from insufficiency of oxygen or from superabundance of carbonic acid in the brain substance itself, or from the transition of the irritation from the respiratory centre upon neighboring, less readily excitable centres (so-called spasm-centres).

If at the same time there be an obstructed flow of the blood from the brain, the spasms may also depend upon this fact (see p. 187).

Convulsions are often absent, even in very rapid kinds of suffocation, as in drowning.

The convulsions do not last until death, but cease, like the dyspnœa and the excitation of the nerve-centres, when the deficiency of oxygen has passed a certain limit (asphyxia).

If suffocation occur gradually, as it commonly does in the observations of

medical practitioners, the convulsions are almost always wanting, and death supervenes, usually without increased frequency of the respiratory movements, as in accumulation of carbonic acid. On the other hand, all mental activity is diminished, especially consciousness, sensation, and motion ; and somnolence, not rarely delirium, decrease of the reflex excitability, etc., occur. Probably these symptoms are mainly dependent upon the carbonic acid poisoning, and in a small measure upon deficiency of oxygen.

That accumulation of carbonic acid in the blood acts paralyzingly upon the nervous system is proven also by RICHARDSON's experiments (*Brit. and For. Med.-Chir. Rev.*, 1863, p. 478) : rabbits and guinea-pigs which were kept in casks filled with pure carbonic acid, or with carbonic acid mixed with an equal volume of air, lost sensation in both cases during the first minute, in the former case only with slight, in the latter with severe convulsions.

The HEART shows in the higher degrees of suffocation, when experimentally produced, a decrease in the frequency of its contractions, sometimes even cessation. The cause thereof is the severe irritation of the medulla oblongata, at the origin of the vagi, in consequence as well of an insufficiency of oxygen as from accumulation of carbonic acid in the blood. Probably other conditions besides irritation of the vagi influence the heart in decreasing the rapidity of its contractions. Increased blood-pressure upon the brain certainly is also capable of irritating the origin of the vagi. Lastly, dilatation of the heart by blood can decrease its contractions and even paralyze it. Suffocation causes death more rapidly if the medulla oblongata or the vagi have been previously severed. The decrease in the rapidity of the heart's pulsations prolongs as much as possible the existence of irritability of the heart's muscles during the impoverishment of the blood by loss of its oxygen, and is therefore a compensatory act. In the last stage of suffocation the vagi become paralyzed, and therefrom the number of the heart's pulsations increase considerably.

According to many, the cause of diminution in the rapidity of the heart's pulsation is ascribed to the increased quantity of carbonic acid in the blood : if through a frog's heart, separated from its body, serum be passed, which is strongly saturated with carbonic acid, the heart's contractions decrease in frequency. It is well known that during the contractions of the impregnated uterus diminution of the fœtal heart's contractions takes place in consequence of irritation of the vagus by the fœtal venous blood. (The same is true of the respiratory movements of the fœtus.)

In the less intense degrees of suffocation there is no diminution in the contractions of the heart ; on the contrary, there is often, in consequence of different complications, an increase in their number.

Those symptoms which appear in the MUSCULAR SYSTEM are due partly to the absence of excitability of the nervous centres, partly to the disturbances in the nutrition of the muscles. They consist mainly in general flaccidity, debility and readily occasioned fatigue, sometimes in strabismus, exophthalmus, etc.

The recent discoveries about fatigue may be considered in this connection. If the power of the muscle depends upon the oxygen which has been accumulated before the muscular exertions (PETTENKOFER AND VOIT), then it is diminished in the condition of suffocation. Fatigue then declares itself partly by the consumption of the oxidizable substance which is contained within the muscle (P. & V.), partly by the accumulation of products from the decomposition of muscular substance within the muscle, especially lactic acid and acid phosphate of potassa (J. RANKE). The excretion of these substances is however decreased by the usually less rapid circulation of the blood and lymph.

Most important and most noticeable is the influence of suffocation on the MUSCULAR COAT OF THE ARTERIES. In consequence of the irritation produced by the blood of suffocation the vaso-motor nerve-centres in the medulla oblongata are excited, and all of the smaller arteries become constricted. Therefrom arises a rapid or a gradual strong dilatation of, and a considerable increase in blood-pressure in the larger arteries and heart.

THIRY has proven, that this constriction of the vessels and increase in the force of the blood occurs through poisoning by carbonic acid (in suffocation, but also when there is no deficiency of oxygen). According to TRAUBE the increase in the blood-pressure is intermittent and regularly rhythmical; according to HERING the rhythm of these rudimentary respiratory twitchings is in accordance with the respiratory innervations. The same phenomena also occur, according to NAWALICHIN, when, in consequence of ligation of the carotids, an accumulation of carbonic acid is produced solely in the cerebral vessels.
LUKOMSKY (*Vtljschr. f. gericht. med.*, 1871, XV., p. 58) found experimentally that in suffocation the lateral pressure of the blood is considerably increased both in the *arteria* and *rena mammaria*, while it is diminished in the *arteria pulmonalis*. According to L., suffocation therefore assists the current of blood through the lungs, brings more blood to the left heart and also increases the force of the blood (in its large circuit). The most important mechanical condition for the occurrence of so-called TARDIEU'S SPOTS (small ecchymoses under the pleura, etc..) is, according to L.'s manometrical experiments, the great increase in the inspiration, which alternates with the active, less sustained movement of expiration.
In suffocating rabbits the fundus of the eye becomes pale in consequence of spasm of the arteries.

Little is known about the condition of the other UNSTRIPED MUSCULAR FIBRES in suffocation. In some cases their movements seem to be increased, in others diminished.

EXOPHTHALMUS is constantly present in suffocation, where it occurs suddenly, as from drowning, strangulation, etc. According to some it is in consequence of the irritation of the sympathetic, whereby is produced contraction of the orbital muscle, according to others it depends upon a venous stagnation, and at the same time flaccidity of the voluntary muscles. Probably both influences act at the same time. In death the exophthalmus disappears more or less completely.

The PUPILS are dilated in suffocation: in consequence of the irritation of the spinal cord, at the cilio-spinal centre (as the dilatation is absent after previous section of the sympathetic). During asphyxia the dilatation of the pupils disappears.

In experiments upon death by drowning, the pupils were first noticed to be contracted, and only later dilated.

The MOVEMENTS OF THE BOWELS are produced, according to S. MAYER and BASCH (see p. 187) by interruption of respiration: in the stage of dyspnœa, in which the small arteries are constricted, the intestine is bloodless and quiet; but as soon as the contraction of the arteries begins to disappear, the passage for the dark blood is opened and movements of the intestine begin. According to O. NASSE the insufficiency of oxygen is not the cause of the anæmic movements of the intestines; the movements of the intestines, occurring when the circulation of the blood through them is cut off, cease if a very weak solution of chloride of sodium be forced through the intestinal vessels.

The TEMPERATURE OF THE BODY is diminished in suffocation. The causes of this are probably numerous. First, the diminution in the quantity of oxygen in the blood, and the consequently diminished oxidations; further the decreased force of the heart; the constriction of the small arteries; moreover the increased cooling of the body by more copious dispersion of

heat and by evaporation, which is due to the dilated veins and capillaries; lastly the decrease of the rapidity of the blood-circulation. The fall in the temperature is present in cases of rapid as well as of common gradual suffocation. Objectively it shows a fall of about .5°–1.5° C.; subjectively it appears as chills, etc. The fall in the temperature is absent when complications arise which tend to increase heat.

SENATOR found a rise of temperature of variable duration in the first stage of the disturbance of respiration, and attributes it to the increased activity of the normal and accessory respiratory muscles, to the heart's increased action, etc. When complete insufficiency of respiration supervenes, the temperature falls. The decrease in the temperature is in consequence of the intense irritation of the medulla oblongata through suffocation. It is almost always absent, when the medulla oblongata has been separated from the spinal cord during the suspension of respiration (HEIDENHAIN, *Arch. f. d. ges. Phys.*, 1870, III., p. 504). At the time when the heart's contractions cease, the temperature again begins to rise: *post mortem* increase of temperature (HEIDENHAIN).

In poisoning by carbonic oxide the temperature sinks 1°–2°, even 3° C., surely in consequence of the deficiency of oxygen. But then it usually remains constant, perhaps on account of the oxidation of the carbonic oxide to carbonic acid. The fall of temperature begins very suddenly: already 30 seconds after the first inspirations it amounts to 0.1°–0.2° C.

The composition of the SECRETIONS, especially of the URINE, in severe uncomplicated, as well as in less severe but usually complicated cases of suffocation is still very little understood. Their qualitatively and quantitatively changed condition may be due to several causes: the diminished quantity of oxygen or the increased quantity of carbonic acid in the blood; alterations in the heart's activity; change in the blood-pressure; alterations (stagnation) in the current of blood through the parenchyma of the glands in question; changes in the albumen of the blood, etc. As regards the urine, its quantity is first increased, and later on decreased. In the common chronic cases of suffocation the latter is usually the existing condition; the urine often contains albumen.

Experiments in respect to this matter were made by OVERBECK and SENATOR. The former (*Oestr. acad. Sitzgsbr.*, 1863, B., p. 189) noticed in attacks of suffocation, which were produced in dogs by complete compression of the trachea, that the urine became albuminous, and at the same time, contained a small number of blood-corpuscles. According to SENATOR (*Virch. Arch.*, XLII., p. 1), the body either, on account of the diminished introduction of oxygen, decomposes less nutritive and tissue-material, and therefore produces proportionately smaller amounts of the final products of metamorphosis (urea, carbonic acid, water, etc.)—as in inanition; or, in consequence of the deficiency of oxygen, it does not produce the final products of metamorphosis, but less highly oxidized substances (uric acid, xanthin, hypoxanthin, creatin, creatinin, sugar, oxalic acid, allantoin, indican), just as in the process of combustion outside the body with insufficient access of air. S. caused dyspnœa to the point of most intense difficulty of respiration by means of mechanical constriction of the trunk. He found almost in all cases a compensatory action, objectively demonstrable by the effects of the tissue-changes, in no wise a diminution. The excretion of nitrogen is never materially decreased, in the first stage of the disturbance of the respiration, but is at least equal to the normal quantity. During the dyspnœa the urine is very abundantly increased, almost to double the normal quantity. This is in consequence of the increased excretion of water; according to S. of increased production of water. It is certainly due mainly to the uninterrupted activity of the respiratory muscles, which are called into action by the obstruction to respiration. Diminished respiration probably causes at first a temporary retardation of tissue-metamorphosis. If the hindrance to respiration be of still longer duration, and cannot be compensated by the respiratory muscles, for example on account of their fatigue, if insufficiency of respiration occur, then there is, beside the cyanosis and the fall of temperature, a diminution in the secretion of the urine. But the material of the body containing

oxygen is decomposed into its final products in the normal manner : therefore there is usually no excretion of less highly oxidized substances. The decrease in the amount of the urine seemed to be more at the expense of the water than of the solid ingredients. Twice the urine contained proportionately large amounts of uric acid : this seems partly to corroborate BARTELS (*Arch. f. klin. Med.*, I., p. 13), who proved that an increase of uric acid excretion not proportionate with the urine was a consequence of insufficiency of respiration. Just as often did the urine contain sugar : this had already been demonstrated by REYNOSO (*Compt.-rend.*, 1851, p. 606). S. did not find any allantoin, xanthin, or hypoxanthin. Neither did he detect blood or albumen.

A direct consequence of the above-mentioned constitution of the blood, and the simultaneous presence of a mechanical stagnation of the blood, is the bluish discoloration of the skin and of the visible mucous membranes, so-called CYANOSIS. It is especially evident in those parts where the superficial vessels are numerous and densely distributed (nails, etc.). It is the more intense the greater the amount of the blood generally, or the greater the proportion of the red blood-corpuscles; for the dark discoloration depends upon the poverty of oxygen in the blood-corpuscles. Therefore cyanosis is proportionately smaller, or occurs only from very intense causes, in those having anæmia, while it attains its highest degree in the *stadium algidum* of cholera (in which the blood is poor in serum, and rich in red blood-corpuscles). Lastly it is the more intense, the greater the accumulation of blood in the veins and capillaries, as in different diseases of the heart and lungs, in cholera : in the former less oxygen is absorbed and less carbonic acid excreted ; in cholera there is a local cause for cyanosis besides in the lungs and heart (their paralysis), far more oxygen is given up and more carbonic acid received in the capillaries of the affected parts of the body (as is the case in a limb which, for instance for the purpose of venesection, has been firmly encircled by a bandage).

Cyanosis is not, as is often stated, produced by the insufficient oxidation of the blood in the lungs.

ASPHYXIA is that state, occasioned by insufficiency of oxygen first of the blood, then of the tissues, in which the movements of respiration and of the heart, and even previously existing convulsions cease. This condition, distinguished in medical practice as the asphyxial stage of many diseases of the air-passages and lungs, is observed most frequently in the last hours of life in laryngeal croup, also in extensive capillary bronchitis, etc. The skin, especially of the face, is less of a blue than of a leaden color, and cool ; the visible mucous membranes are also bluish-gray. The previous anxious expression of the features becomes indifferent and dull ; the eyelids close ; the pulse becomes small, very frequent, irregular, superficial. All bodily movements are feeble. The pupils are normal or contracted. At last somnolence, anæsthesia, and death (which is often preceded by convulsions) occur.

Of great practical importance are the COMPENSATIONS which appear with most slight causes of suffocation, and which prolong life as well as make the condition, through diminished demands upon the organism, more endurable. In cases, on the contrary, in which the causes of suffocation occur suddenly and are intense, the appearance of these compensations is not capable of prolonging life. The same is true in cases of the more intense poisoning by carbonic oxide.

The most important compensation is DYSPNŒA in both its forms (see p. 561) : the more frequent or deeper inspirations neutralize the effect of a

diminished quantity of oxygen in the atmospheric air, as also of most of
those causes of suffocation mentioned in 1, for the deeper the ventilation
of the lungs, the greater the exhaled quantity of carbonic acid.   Another
compensation is obtained by an accommodation of the consumption of
oxygen to the amount of oxygen inhaled, and accordingly a diminution of
all actions of the organism which necessitate oxidation.

Furthermore the changes in the circulation act compensatorily upon
most of the causes mentioned in 1 and 2 : first, the acceleration of the
blood-current, whereby more blood-corpuscles are brought into contact
with the air of the lungs in a given time, which probably induces an in-
crease in the absorption of oxygen and in the excretion of carbonic acid ;
secondly, the more frequent decrease of the rapidity of the blood-current,
in consequence of which the excitability of the heart's muscles is prolonged
as much as possible during the impoverishment of the blood in oxygen.
Lastly the increased pressure of the blood, or rather the dilatation of the
capillaries, which appears in consequence of the constriction of the small
arteries, is of importance, for thereby the area of contact between blood
and air is enlarged, and the pressure, which acts upon the carbonic acid
of the blood, increased.

If the suffocation be of longer duration, and is caused by diseases of
lungs and heart, dilatation and hypertrophy of sometimes the whole heart,
sometimes of a single division, are almost always produced.   In respect to
this, hypertrophy of the normal or of the dilated right ventricle is espe-
cially important : partly on account of the increase in the pressure of the
blood and the consecutive increased exchange of gases in the alveolæ of
the lungs, partly on account of the prevention of stagnation in the veins
of the body, etc.

According to THIRY, LUDWIG and others, the resistance to the efflux of blood
increases by the constriction of the small arteries, and therefrom arises an accumula-
tion of the blood in the large arteries, and so increased blood-pressure ; but the
diminished afflux of blood to the capillaries causes a diminished rapidity in these
and in the veins.   DOGIEL and KOWALEWSKY (*Arch. f. d. ges. Phys.*, 1870, III., p.
489) also found in cases of suffocation an increase of the arterial blood-pressure and
a rapid decrease in the rapidity of the arterial blood-current, to increase again in
the subsequent period of respiration.   According to HEIDENHAIN, on the contrary,
the blood-pressure and the rapidity of the blood-current increase on irritation of
the vaso-motor nerves.   According to this the consumption of oxygen and the
production of carbonic acid in the tissues would increase, as also the temperature.

In the lower degrees of poisoning by carbonic oxide a return to the normal condi-
tion takes place, in consequence of the oxidation of the carbonic oxide to carbonic
acid by the oxygen which still remains in the blood.

The question of how long after cessation of respiration and circulation a
resurrection is possible, is of especial practical interest.   The latter differs
according to individual peculiarity, the cause of suffocation, etc.   There-
fore no general conditions can be mentioned.   The decrease in the quantity
of oxygen can be endured for a longer period by human beings and animals
born apparently dead (by hibernating animals), by people in a fainting
condition, or under the influence of chloroform, longer than under usual
circumstances.

According to TARDIEU, a dog can return to life without any artificial means, after
four minutes of suffocation, if caused by mechanical closure of the trachea,
while one and a half minutes by drowning are fatal (because water penetrates into
the lungs).   The heart requires, to maintain its activity, blood containing oxygen,
but not every second, as it is always charged with a certain quantity of oxygen :

this explains the fact that the movements of the heart can continue for three minutes and more, in a dog suffocated by mechanical means, after the last effort at respiration (TARDIEU).

Some forms even of acute suffocation present many deviations from the above description. We can mention only a few of the better known and more important ones.

In poisoning by CARBONIC OXIDE there are present, besides the usual phenomena of suffocation, the specific poisonous influences upon the whole organization, especially the brain: loss of consciousness, serious phenomena of the senses of sight and hearing, frequently vomiting, quite often diarrhœa, etc. Besides this, numerous individual differences occur, so that in the simultaneous poisoning of several people one or more may die, of the others some may present light, and some severe phenomena of intoxication.

According to TRAUBE (*Verh. d. Berl. med. Ges.*, 1866, I. ; *Ges. Beitr.*, 1871, I., p. 392), carbonic oxide acts injuriously in two ways: first, by diminishing the quantity of oxygen needed for the expiratory nervous system ; secondly, by forming, in combination with hæmoglobin, a poisonous substance, which excites and paralyzes the nerve-centres. Carbonic oxide excites the heart's inhibitory nervous system : the diminished frequency of the pulse in the first stage of intoxication is a result of this action. It excites the centre of the vaso-motor nervous system : the increase in the frequency of the pulse, which precedes its primary diminution, is a result of this action. It weakens the heart's muscle : decrease of the pressure in the beginning of intoxication is the consequence. According to KLEBS (*Virch. Arch.*, XXII., p. 450), atony of the walls of the vessels occurs, in consequence of which the pressure of the blood and the rapidity of the circulation diminish, and there follows paralysis of the heart; furthermore there is an atony of the greater part of the unstriped muscular fibres (the iris, stomach, intestine, bladder). POKROWSKY (*Ib.*, XXX., p. 525). Compare also FRIEDBERG, *Die Vergiftung durch Kohlendunst*, 1866.

Poisoning by CARBONIC ACID gives, besides the usual phenomena of suffocation, fewer specific symptoms, by which the poison can be detected, than that by carbonic oxide.

Death by DROWNING is understood from the symptoms, etc., observed in a series of experiments.

According to FALK'S (*Virch. Arch.*, 1869, XLVII., p. 39) experiments, respiration ceases as soon as the animal enters the water (being partly a psychical effect, partly in consequence of the irritation of certain nerve-groups of the skin). Thereupon (second stage) an almost normal inspiration occurs, followed by a powerful expiration ; then another deep inspiration and a similar expiration ; then the inspirations grow deeper and deeper, but the expirations become less powerful ; the pauses between the respiratory acts become longer, until all respiratory movement ceases. This cessation is due to the paralysis of the respiratory centre. The glottis is not closed. In the third stage, the stage of asphyxia, strong dilatation of the pupils and exopthalmus appear ; there are no respiratory movements, no consciousness, no reflex irritability. Then follow a few very labored inspirations and superficial short expirations. In the fourth stage the pupils again contract, the exophthalmus disappears ; the heart ceases to beat.*

POST MORTEM EXAMINATIONS of pure cases of common suffocation show, beside the already-mentioned condition of the blood a large quantity of it within the right heart, the lungs and veins of the body, and, in consequence, nearly always an intense hyperæmia of the capillaries of the lungs,

* Consult : *Report of Committee on Suspended Animation, in Med.-Chir. Trans.* XLV.—P. BERT, *Leçons sur la phys. comp. de la respiration.* Paris, 1870.—[ED.].

the air-passages, the organs of the head and abdomen, especially the kidneys.   In the serous coats, especially in the pleura and pericardium, recent slight hæmorrhages are found: they occur in consequence of dyspnœa and the increased arterial blood-pressure.   The left heart is always empty if death by suffocation occur rapidly; if not it contains more or less blood. The air-passages often contain foamy fluid in abundance, not rarely mixed with blood.   The lungs are voluminous in consequence partly of hyperæmia, partly of serous infiltration.

In cases of poisoning by carbonic oxide the blood is almost always of a light red color (dark only when the carbonic oxide has been entirely changed into carbonic acid); numerous bright red spots, of varying size, appear on the skin.   Furthermore, here as well as in most cases of poisoning, parenchymatous clouding of the muscles, the large glands, etc., appear.

In cases of death from drowning, the fluid in which it occurred is found in the air-passages and lung-cells; only a small part of the fluid contained in the latter being blood-serum.   The fluid enters these locations only in a short period before the agony, mainly during the agony; according to experiments, deep inspirations and feeble expirations are said to occur in the last stage of asphyxia.   Sometimes death by drowning occurs very suddenly without any deep inspirations before the agony, and then no fluid penetrates from without (so-called apoplectic death by drowning).

XIII. URÆMIA.

(Febris urinosa.   Typhus urinosus.   Urodialysis.)

BRIGHT, Rep. of Med. Cases, 1827.—CHRISTISON, On Gran. Degen. of the Kidneys, 1829, Transl., 1841.—BERNARD et BARRESWIL, Arch. gén., 1847, XIII., p. 449.— STANNIUS et SCHEVEN, Arch. f. phys. Heilk., 1850, IX., p. 201.—FRERICHS, Arch. f. phys. Heilk., 1851, X., p. 399; Die Bright'sche Nierenkrankh., 1851.—SCHOTTIN, Arch. f. phys. Heilk., 1852, XI., p. 88; 1853, XII., p. 170.—VOGEL, Virch. Path., 1854, I., p. 448.—STOKVIS, Nederl. Tijdschr., 1860, IV., p. 513.—HAMMOND, Am. Journ. of Med. Sc., Jan., 1861.—TRAUBE, Med. Centralz., 1861, No. 103; Berl. Klin. Wschr., 1867, No. 47.—OPPLER, Virch. Arch., 1861, XXI., p. 260.—PETROFF, Virch. Arch., 1862, XXV., p. 91.—ROSENSTEIN, Die Path. u. Ther. d. Nierenkrkh., 1863; 2. Aufl., 1870.—PH. MUNK, Berl. klin. Wschr., 1864, No. 11.—KÜHNE et STRAUCH, Med. Ctrlbl., 1864, No. 36 et 37.—PERLS, Koenigsb. med. Jahrb., 1864, IV., p. 56.—ZALESKY, Unters. üb. d. uräm. Process, etc., 1865.—MEISSNER, Ztschr. f. rat. Med., 1866, XXVI., p. 225.—VOIT, Ber. d. Bayerischen Acad., 1867, I., p. 364.—Ztschr. f. Biol., 1868, IV., p. 77.—BARTELS. In Volkm.'s klin. Vortr., 1871, No. 25.—HAMPELN, Dorp. med. Z., IV., p. 105.

URÆMIA is an usually acute condition, nearly always accompanied by typhoid symptoms, frequently by vomiting, loss of consciousness, somnolence, convulsions, etc., which occurs especially in the course of diffused nephritis (Morbus Brightii), in consequence of disturbed activity of the kidneys, especially of retention of urine, and probably of all its ingredients, but mainly of urea, uric acid, creatinin and extractive matter.

The above opinion is based partly upon clinical and pathologico-anatomical observation, and partly upon numerous experiments, in which animals were deprived of both kidneys, or both ureters were ligated.   The results of these experiments were phenomena similar to those of uræmia in man, and death.   In the blood and in several tissues, especially the muscles, urea was found, and a number of other substances were considerably increased (extractive matters, potassa salts, creatin): according to some after both operations, according to others only after the ligation of

the ureters. Furthermore there appeared within the tissues substances which are not there normally, mainly such, like creatin, as must be considered final physiological products of the decomposition of albumen.

Normal blood contains in 100 grm. 16–20 mgrm., uræmic blood 40–60 and more of urea. Moreover there is in the latter an increase of extractive matters. MEISSNER also discovered an abundance of succinic acid in it. Many have found after double nephrotomy or after ligation of both ureters a considerable increase of urea in the blood. In animals (dogs) who vomited, this was not constant. Furthermore urea was discovered in the liver, brain, and muscles, organs in which, excepting the liver (MEISSNER), they do not occur normally.

In the first period of the knowledge of uræmia the opinion was held, that the urine was in toto the cause of the disease : as soon as it was prevented from being excreted by the kidneys, it would be in a vicarious way by the stomach and intestine, by existing wounds and ulcers, etc. ; a certain kind of metastasis occurred. Injections of urine into the vessels produced similar symptoms, if the urine had not been filtered ; but if it were filtered, or if the urea, which was considered especially obnoxious, was injected alone, it had no effect, because the kidneys excreted it too rapidly (VAUQUELIN and SÉGALAS). After injections of the pure urea even, HAMMOND and GALLOIS pretend to have noticed uræmia ; but the large majority of experimenters (STANNIUS, FRERICHS, HOPPE-OPPLER, PETROFF, MUNK) did not observe it, excepting when very considerable quantities had been injected. The latter is also the case in the later studies by FALCK (*D. Kl.*, 1871, No. 41 ff.) and GOEMANN (MEISSNER, *Z. f. rat. med.*, CXXVI., p. 241). O. REES, BRIGHT and others found blood very rich in urea without the presence of uræmia. (Compare, *infra*, experiments on feeding by VOIT.)

FRERICHS holds that not the simple retention of the ingredients of the urine, especially of the urea, is the cause of uræmia, but that accumulated in the blood it must be changed within the vascular system by the agency of a fermenting body into carbonate of ammonia in order to induce uræmia : for (1) the latter produces, when injected into the blood, symptoms very similar to those of uræmia, and (2) this salt is present in the blood during the uræmic condition as well of the sick as of nephrotomized animals, but absent in healthy blood. This theory was accepted generally for several years. But already in 1853 SCHOTTIN proved that pure urea (not carbonate of ammonia) appeared upon the skin and in the secretions with uræmic phenomena in the typhoid stage of cholera. SCH. proved furthermore that similar symptoms occur after injection of other substances. as carbonate of soda, sulphates, etc. (though this is denied by later experimenters. as PETROFF, ZÜLZER, and others). Moreover, HOPPE-OPPLER, as well as MUNK and VOIT, deny that the phenomena produced by carbonate of ammonia and those by uræmic poisoning are alike. (PETROFF on the contrary saw after injections of carbonate of ammonia. and after extirpation of the kidneys, attacks quite similar to those of uræmia.) The second point of FRERICHS' theory was also disputed. HOPPE-OPPLER detected only urea in the blood of persons suffering from uræmia, as also in that of nephrotomized animals. but they failed to find any carbonate of ammonia. The latter is corroborated by KÜHNE-STRAUCH, as also by ZALESKY. (PETROFF on the contrary says that he found it after nephrotomy.) Whether it appears in the blood of uræmic people, is doubtful. Lately SPIEGELBERG and GSCHEIDLEN found it in the blood of a woman suffering from eclampsia.

According to FRERICHS the carbonate of ammonia originates within the blood, while according to BERNARD, STANNIUS, TREITZ and others the urea is decomposed into carbonate of ammonia within the stomach and intestines by the action of the present urea ferment, and only thence the ammonia is absorbed by the blood. VOIT also demonstrated, that a transformation of urea into carbonate of ammonia only takes place within the intestinal canal : the contents of the intestines of uræmic animals as well as the ejected matter from the stomach before death have an alkaline reaction and the urea has disappeared.

Consequently, FRERICHS' hypothesis is either false. or at least does not explain all cases. For (1) the symptoms appearing after injections of carbonate of ammonia are not entirely the same as those of uræmia ; (2) it is not proven that the blood of uræmic animals contains carbonate of ammonia (STRAUCH-KÜHNE) ; the urea in the body does not change so readily into carbonate of ammonia. VOIT searched unsuccessfully for carbonate of ammonia in the expired air of animals after nephrotomy or ligation of the ureters ; (3) it is not demonstrated that the carbonate of ammonia is

only produced by the decomposition of urea. VOIT demonstrated its presence within the urine by feeding healthy animals with it; (4) SCHOTTIN found also a large quantity of creatinin in the blood of uræmia, and noticed its excretion with the urine in favorable cases; in unfavorable cases the creatin and creatinin would accumulate in the fluids of the body. SCH. believes that the action of uræmia consists mainly in a disturbance of general nutrition and especially of the muscles; (5) clinical observation speaks against FRERICHS: uræmic phenomena occasionally occur while the urine is excreted in normal quantity and urea in only slightly diminished amount; occasionally when the excretion of urine and of urea remains relatively the same; finally occasionally when there is abundant excretion of urine and of urea, while they may not appear even with complete ischuria of long duration (observations of CHRISTISON, LIEBERMEISTER, BIERMER, ROSENSTEIN and others).

ROSENSTEIN (*Virch. Arch.*, 1873, LVI., p. 383) concludes from experimentation on animals, etc., that carbonate of ammonia, introduced into the blood in sufficient quantity, can always only produce the same series of phenomena, those of epilepsy (probably by direct influence upon the nerve-substance of the cerebral centre of convulsions), while the agent which produces uræmia induces the phenomena of epilepsy, but besides those of coma, convulsions and delirium. But even if the uræmic condition resemble that of poisoning by ammonia, and even if ammonia be found in the blood, the former is not dependent upon the latter, because the same phenomena occur in man without the presence of ammonia in the blood, and because no proportion between the intensity of the uræmic phenomena and the quantity of ammonia exists in experiments upon animals.

To these chemical hypotheses TRAUBE, previously OWEN REES as well, opposed a physical one. According to him the serum of the blood in *morbus Brightii* is more liquid and more disposed to transudations; simultaneously hypertrophy of the left ventricle of the heart arises in consequence of the abnormally high tension of the aorta (fulness of the pulse, etc.). If from any cause the liquefaction of the serum or the tension of the arteries suddenly increases, œdema and anæmia of the brain follow, and in consequence thereof the symptoms of uræmia are produced. If only the cerebrum becomes œdematous and anæmic, simple coma arises; but if at the same time the mesocephale also becomes anæmic, convulsions occur; if only the latter becomes anæmic, convulsions merely are produced. MUNK found the brain œdematous after nephrotomy, and its gyri collapsed. He tried to support this hypothesis, which VOIT and others do not acknowledge, experimentally. If he ligated the ureters and one jugular vein of a dog, and then injected water into the carotids, severe convulsions, similar to the uræmic ones, and coma set in; the brain was usually anæmic and œdematous. But the uræmic phenomena appeared not at all or very late, if, after ligation of the ureters or extirpation of the kidneys, etc., the carotids were tied. ROSENSTEIN (*Monatschr. f. Gebrtsk.*, XXIII., p. 413) explains eclampsia in the same way. OTTO (*Beitr. z. L. v. d. Eclampsie*, Dorpat, 1866) also. According to E BIDDER (*Holst. Gynäk. Beitr.*, 1867, II.), injections of water only produce convulsions and coma, when the lateral pressure is increased to four or five times the normal. Even a lateral pressure, equivalent to a column of mercury of 500–700 mm., was well borne, if B. injected blood-serum in place of water. VOIT and others, and also many pathological anatomists, did not find the quantity of water in the brain of nephrotomized animals increased.

Still it remains most probable that diminished excretion of all or almost all ingredients of the urine produces uræmia.

OPPLER found, after extirpation of the kidneys, or after ligation of both ureters with subsequent injection of urea, an enormous increase of the extractive matters of the blood and a large amount of creatin and leucin in the muscles. According to him, the products of the decomposition of muscles increase in enormous amounts, and accumulate in consequence of suspended activity of the kidneys. They are also probably produced in the spinal cord and brain, and are the cause of uræmia.

The experiments of ZALESKY on birds and snakes make it probable that the retention of urea is not the only cause of uræmia: both these classes of animals, who, as is well known, do not excrete any urea, showed well-marked symptoms of uræmia after nephrotomy as well as after ligation of the ureters. According to MEISSNER, urea produces, when injected into the blood of rabbits, comatose symptoms only in doses of at least one to two grm. Creatin injected into the blood has no results, and is rapidly excreted by the kidneys. Creatinin produces great fatigue, and twitchings on attempts to move.

VOIT rejects all former chemical and the physical hypothesis of uræmia, and comes to the conclusion that it is not produced by retention of urea only, but also of uric

acid, potassa salts and other ingredients of the urine, and that thereby all products of decomposition not gaseous are not only retained in the blood but also in the organs; that the interchanges between the blood and the minutest divisions of the organs cannot take place if the products of decomposition, which arise from nutrition, etc., are not excreted. (Compare PERLS, l. c.) VOIT supports this opinion by experiments upon animals, and upon the previous examinations of the relation of creatin and creatinin to urea in the animal economy. Fresh normal muscle contains creatin, traces of creatinin, but no urea (as ZALESKY believes). But the latter is present in the muscles of nephrotomized dogs in considerable quantity: 0.12–0.14, even 0.63 per cent. In normal circumstances urea originates within the organs, especially the muscles; creatin and creatinin are not changed into urea. Contrarily to others, V. found after nephrotomy, if the animals survived the operation as long as after ligation of the ureters, and if the urea was not excreted by any other organs, just as large a quantity of urea in the blood (in accordance with MEISSNER, who attributes the deficiency of the urea to its expulsion with the vomiting which always occurs in dogs) and in the organs, as after ligation of the ureters merely (in opposition to ZALESKY); there was no difference in the two operations as regards the amount of creatin in the muscles (contrary to ZALESKY, who always found more creatin in the muscles after nephrotomy than after ligation of the ureters). According to VOIT, small dogs can be fed with large amounts of urea without the occurrence of any remarkable phenomena in them, provided they can take water: for urea requires, just like the neutral salts, a certain amount of water for its elimination. But if the excretion of urea is interfered with by the abstraction of water, the most intense uræmic phenomena appear.

CAUSES OF URÆMIA. These may be any disease of the kidneys, in which the secretion of urine is more or less prevented: inflammations therefore of the kidney-tissue, those combined with formation of abscesses, but more especially the different so-called albuminous infiltrations, which are designated diffused nephritis or *morbus Brightii*; its primary as well as the secondary forms. Another cause is formed by all those affections which cause a diminution or complete cessation of the excretion of urine, be their origin in diseases of the urinary passages, or of their neighboring parts: hydronephrosis, pyelitis, cystitis, stricture of the urethra, diseased prostate gland, paralysis of the urinary bladder, etc.

Uræmia occurs much more frequently in the course of granular kidney than of the chronic inflammatory swelling of the kidney (so-called second stage of *morbus Brightii*); the minute quantity of excreted urine of the latter contains a much larger percentage of urea than the abundant watery urine of the former (BARTELS). It is very rarely that uræmia occurs from fatty kidney. In Asiatic cholera the secretion of urine ceases entirely in the stage of asphyxia or *stadium algidum* (in consequence of the diminished blood-pressure); in the stage of reaction and in the typhoid stage the urine is albuminous, poor in urea, etc. (In the latter case in consequence of the croupous nephritis or the great loss of water from the intestines.)

Numerous pathologico-anatomical examinations show that in cases of uræmia both kidneys are always diseased, mostly to the same, more rarely in different degrees: if with severe disease of one kidney the other be normal, no disturbance occurs in the excretion of urine. ROSENSTEIN (*Med. Ctrlbl.*, 1871, No. 23) found the excretion of the urine after extirpation of one kidney the same on the two consecutive days after the operation as before it.

Why during the above-mentioned diseases, under apparently the same conditions, uræmia is now present, now absent; why there is no uræmia after ischuria of several days' duration, without simultaneous vomiting or diarrhœa, is not understood. In general, uræmia arises the more readily, the more sudden, and the more complete the cessation of se- or excretion of the urine is, as also the more robust the individual was before the attack of the disease in question (cholera, scarlatina); and, lastly, the greater the accumulation of excrementitious matter was in their body (in diseases

attended with high fever, pyæmia, etc.). Generally the occurrence of uræ-mia, in *morbus Brightii*, is hastened by the absence of dropsy: perhaps because a large amount of urea is taken from the circulation by the dropsi-cal effusion which usually contains more of the urea than the blood. Uræ-mia never occurs as long as there exists a high degree of dropsy, but is occasionally produced when the effusion suddenly disappears, spontaneously or in consequence of medication ;—hot baths.

BARTELS holds the sudden intermingling of the blood with the products of the retrogressive metamorphosis, as they are contained in the dropsical fluid, to be the cause of uræmia.

In the uræmia of cholera the tension of the vascular system is decreased by the enormous loss of water and the diminution of the heart's activity. Thereby the blood not only loses water, but becomes surcharged with urea, which it absorbs from the tissues. (KAUP AND JÜRGENSEN, *Arch. f. klin. Med.*, VI., p. 55.)

The outbreak of uræmic symptoms is prevented by excretion of the urea and the other ingredients of the urine into the stomach and intestines (by vomiting and diarrhœa), perhaps also upon the skin.

NYSTEN, MARCHAND, LEHMANN, and others found urea in the stomach after nephrotomy ; BERNARD, STANNIUS, and others found carbonate of ammonia in it.

The SYMPTOMS OF URÆMIA are usually not so characteristic that a diag-nosis is possible without the knowledge of the previous disturbance of the se- or excretion of urine. Its excretion is generally diminished, even entirely suspended, rarely normal, still more rarely increased. According to each special cause the urine has a different composition : most frequently it is albuminous ; its quantity of urea is mostly decreased (instead of about thirty grm. in twenty-four hours, ten to seven grm.) rarely normal, very rarely increased.

From the fact of the decrease of the urea it cannot be positively concluded that there exists retention of urea. As most of these patients are anæmic, it is possible that there is a diminished production of urea (HAMPELN, l. c.).

The FUNCTIONS OF THE BRAIN are disturbed, most frequently with paralysis : general mental inactivity, apathy, impaired consciousness or its entire loss ; drowsiness or somnolency ; occasionally amblyopia or even amaurosis with power of reaction of the pupils, difficulty of hearing, diminished sensation. At other times there appear symptoms of irritation of the brain, either simultaneously or separately : different forms of delirium, delusions of the senses ; especially frequent are attacks of partial, more frequently of general convulsions, usually similar to epileptic, more rarely to tetanic seizures ; usually attended by unconsciousness. In the beginning headache frequently exists, usually very severe.

The immediate cause of the above-mentioned brain-phenomena is still unknown. It is even probable that several substances occasion all or part of these phenomena : the greater amount of water in the blood, the urea, the potassa salts. According to RANKE (*Grdz. d. Phys.*, 1872, p. 531), urea causes an irritation of the controlling centre of reflex action, wherefrom gradually a paralysis of the entire peripheral reflex apparatus is developed ; perhaps it also acts paralyzingly upon the nervous will-organ.

As regards the ORGANS OF DIGESTION vomiting especially is a constant symptom, diarrhœa less so. The vomited matter consists first of the ingesta

and has an acid reaction; later on it consists of mucus or watery substances, and has a neutral or alkaline reaction, and then occasionally has an ammoniacal odor. The diarrhœa is occasionally profuse and obstinate. The appearances of the digestive passages are probably due to the irritation by the urea excreted into it, or by the carbonate of ammonia which is produced from it.

The vomited matter contains urea according to BERNARD and BARRESWIL, as also according to HAMMOND.

The TEMPERATURE is usually increased in acute cases, and the skin is usually dry. The pulse has no constant characteristics; usually it is quickened and hard; sometimes it is slower than normally. Respiration is usually quickened; occasionally there is dyspnœa. The presence of ammonia in the expired air of the person suffering from uræmia is frequent, but not constant, and is also often found under other circumstances.

(SCHOTTIN, l. c.—REULING, Ueb. d. Ammoniakgehalt d. expir. Luft. u. s. w., Giessen, 1854.—HAMMOND, Amer. Journ. of Med. Sc., Jan., 1861.)

The PERSIPRATION contains, besides other substances, urea which is often excreted, usually only shortly before death, upon the uncovered portions of the skin, especially the forehead and the upper part of the face, by evaporation of the water in which it is dissolved, and then forms a frost-like covering.

The COURSE OF URÆMIA is variable. Sometimes it begins almost unnoticed with but light symptoms; sometimes the symptoms are more marked and aggravated, and sometimes it commences suddenly in the most intense form. The first mentioned form is often overlooked, the second kind can easily be confounded with typhoid fever, the last has some similarity to hæmorrhage in the brain, or with epilepsy, or with an acute poisoning (by opium, belladonna, alcohol, lead), or with cholera. Its course is acute, subacute, or chronic, rarely regular, frequently interrupted by severe attacks (so-called uræmic attacks); occasionally attacks occur, separated by perfectly free intervals.

The termination of uræmia is almost always fatal. The single attacks not rarely pass over entirely or almost entirely; probably by the separation of the injurious substances by the kidneys or stomach, or intestinal mucous membrane, or lungs or skin, or by their decomposition within the body.

AMMONLÆMIA.

TREITZ, Prag. Vjschr., 1859, IV., p. 160.—JAKSCH, ib., 1860, II., p. 143.

AMMONLÆMIA is that change of the blood which arises from retention of urine, especially of urea, and the consequent metamorphosis of the latter into carbonate of ammonia, which gets into the blood. The retention of the urea usually is the consequence of any retention of urine (strictures of the urethra, enlargement of the prostate, paralysis and chronic catarrh of the urinary bladder, suppurating pyelitis). It causes an irritation of the mucous membrane of the bladder, an increased production of mucus or even of pus, and a change of urea into carbonate of ammonia, which is usually produced by a specific ferment which is introduced from without. More rarely ammoniæmia occurs simultaneously with uræmia: then it is

possible for the urea, excreted into the intestines, to change into carbonate of ammonia, and the latter to cause ammoniæmia.

(Compare FRERICH's hypothesis, p. 571.)
Experimental observations in regard to ammoniæmia have only been made rarely and usually indirectly. According to OPPLER, restless movements, vomiting, severe convulsions are induced by injection of carbonate of ammonia into the blood. VOGEL corroborates this. ZALESKY found that after ligation of the ureters there were exhalations of a urinous odor even before life was extinct; the same odor appeared when the abdomen was opened. But neither nephrotomy nor ligation of the ureters had any influence upon the quantity of ammonia contained in the blood. ROSENSTEIN (see p. 572) denies any connection between ammoniæmia and poisoning by carbonate of ammonia.
The mucus-like masses in certain cases of inflammation of the bladder, where alkaline fermentation of the urine has commenced within the urinary passages, do not consist of mucus which has been separated from the mucous membrane of the bladder, but is a product of the influence which the carbonate of ammonia, which has been developed from the urea, exerts upon the pus-corpuscles contained in the urine. Usually the ferment is introduced into the urinary bladder by means of the catheter (FISHER-TRAUBE, *Berl. klin. Wschr.*, 1864, No. 2. Compare TEUFFEL, *Ib.*, No. 16).

The SYMPTOMS OF AMMONIÆMIA are: first, the mucous or muco-purulent contents, as well as the strongly alkaline condition of the urine; the large quantity of ammonia contained in the expired air; occasionally vomiting, with diarrhœa or constipation; remarkable dryness of mouth and throat; dry skin; usually a high temperature; full possession of consciousness.

JAKSCH makes a distinction between acute and chronic ammoniæmia: in the first there are usually vomiting (which in an unfavorable case is followed by fever), great muscular prostration, rapid alteration of the face and sopor; in the latter gastric symptoms, similar to those of chronic catarrh of the stomach, occur, sometimes combined with severe intermittent chills. Dropsy is said never to be present; neither are convulsions or disturbances of sight.

The termination is rarely in health; usually after increasing emaciation and cachexia death occurs.
In the corpse the urinary passages, more particularly the kidneys, present different changes according to the cause. In the intestinal canal there is always chronic catarrh.

According to TREITZ, the intestines contain an abundant greenish-yellow, thinly mucous, neutral and alkaline fluid with an ammoniacal odor, usually without fæces. Their mucous membrane is œdematous, in a condition of acute or chronic blennorrhœa; it frequently presents ulcers similar to those of dysentery.

HYDROTHIONÆMIA, AND HYDROTHION-AMMONIÆMIA

consist in the entrance into the blood of sulphuretted hydrogen, or sulphuretted hydrate of the sulphate of ammonia, which is produced in the stomach and intestines in consequence of errors of diet and of catarrh, or in the peritoneal cavity after perforation of the bowel. Therefrom are produced symptoms similar to those in poisoning by these gases: general collapse, dizziness, pallor, frequent, but very small pulse, rapid, superficial respirations; the urine gives the reaction of sulphuretted hydrogen (acetate of lead paper). The attacks pass away rapidly or not, according to the cause, or death ensues. In *post mortem* examination, great rigidity, brown'sh-red dry muscular fibres, incomplete coagulation of the blood, and hyperæmia of the pelves of the kidneys are found.
Compare BETZ, *Memor.*, IX., No. 7.—SENATOR, *Berl. kl. Wschr.*, 1868, No. 24.—EMMINGHAUS, *Ib.*, 1872, No. 40 et 41.

ACETONÆMIA.

PETTERS, *Prag. Vtljschr.*, 1857, LV., p. 81.—KAULICH, *Ib.*, 1860, LVII., p. 58.—BETZ, *Memorabilien*, 1861, VI., *No.* 3.—CANTANI, *Il Morgagni*, 1864, VI., p. 365 et 650.

Acetonæmia is a morbid state which occurs in various conditions (diseases of stomach and intestine, intoxication, many febrile diseases, most frequently diabetes), and which is characterized by the presence of acetone in the blood, by a peculiar odor of the exhalations from mouth and lungs, as well as of the urine, and by diverse well-marked nervous disturbances, which sometimes consist of depression, sometimes of excitation. The symptoms presented by the heart and the organs of respiration are not constant. The mucous membrane of mouth and throat are always red, dry, and more or less glistening and hot.

Acetone, a derivative of acetic acid, is produced according to some in the stomach and intestines, according to others in the liver and thence is carried into the blood: probably it is formed from grape-sugar. It was first discovered in the urine, later also in the stomach and blood of those suffering from diabetes, then also in those having measles, scarlatina, typhoid fever, pneumonia, etc.

URIC ACID DYSCRASIA.

BARTELS, *D. Arch. f. klin. med.*, 1865, I., p. 13 (see Suffocation, p. 557).

The existence of a so-called uric acid dyscrasia or diathesis is still doubtful.

The smaller or greater formation of uratic deposits, which very frequently occur in the urine of those sick with fever, in acute articular rheumatism, in several diseases not accompanied by fever, is no proof of an increased production of uric acid. The cause of this is usually in the presence of other acids, which precipitate the uric acid as such or as uric acid salts.

An actual increase of the excretion of uric acid really occurs: either from increased production of uric acid (with simultaneous increased production of urea, consequent to an increased consumption of albuminous substances, as in fever); or from diminished oxidation of the uric acid formed in normal quantity (as in leucocythæmia, chlorosis, and probably also in poisoning by coal-gas). The consequences to the organism are probably not injurious. Concretions may be formed within the urinary passages. *Vide* p. 319.

TRUE GOUT, PODAGRA, consists according to some of the decreased excretion of uric acid by the urinary organs and an accumulation of it within the blood, moreover of a deposit of urate of soda in the joints, sometimes also beneath the skin, in the cartilage of the ear, etc. According to others, there is an actual increased production of uric acid in the gouty; but it leaves the body if the kidney is in normal condition. The diminished excretion of uric acid by the kidneys is said to be due to the fact than an acid is produced either in consequence of an hereditary tendency, or more commonly from the immoderate use of meat and strong drink with little bodily exercise, which acid has a greater affinity for soda than uric acid. The consequent precipitates of urate of soda in the canals of the medullary substance of the kidney impede the excretion of urine and favor the absorption of uric acid. If this impediment to the excretion of uric acid occur suddenly an attack of gout arises.

See p. 319. TRAUBE, *Berl. klin. Wochenschr.*, 1865, No. 48. When ZALESKY (*Unters. üb. d. uräm. Process, u. s. w.*, 1865) ligated the ureters of a bird, death occurred after 20–37 hours. Dissection showed abundant deposits of uric acid salts upon the surface of the tissues and of all organs and within their parenchyma, excepting the brain. Their quantity depended upon the length of the duration of the animal's life. The salts were not deposited within, but between the cells. Upon the serous membranes they were in a crystallized condition ; and their lymphatic vessels were as it were injected with a white glistening substance. The blood-coagula of the heart and vessels often contained small particles of uric acid salts. All joints, those of the older animals in especially large quantities, contained infarctions of uric acid. The kidneys were always infiltrated first and most abundantly with uric acid salts. The blood contained 0.44–1.3% of uric acid, that of the animals which died after 26–36 hours had double the quantity of those killed after 12–24 hours.

SCHRÖDER V. D. KOLK (*Nederl. Lanc. Juli et August*, 1853) found in the examination of the greatly affected hands of a gouty patient not only large deposits of urate of lime in the tendons of the flexors and extensors of the fingers, as well as in the ligaments, but also beneath the skin in large lumps, so that several digital nerves were here and there entirely surrounded and penetrated by urate of lime. The veins appeared in the dried skin, from the large amount of lime deposited in their course, as white branches, while the arteries were normal. Wherever the skin was most abundantly saturated with urate of lime, there the veins and capillaries of the skin were also most abundantly filled with the same salt.

XIV. DIABETES MELLITUS.   MELLITURIA.   GLYCOSURIA.

TH. WILLIS, *Pharmac. ration.*, 1674, IV., C. 3.—ROLLO. *Cases of the Diab. Mell.*, 1798.—NASSE, *Unt. zur Path. u. Phys.*, 1835 ; *Arch. f. phys. Heilk.*, X., p. 72.—PROUT, *On the Nat. and Treatm. of Stom. and Urin. Dis.*, 1840.—BOUCHARDAT, *Ann. thérap.*, 1841-42-46-48.—TRAUBE, *Virch. Arch.*, 1851, IV.—PETTERS, *Prag. Vjschr.*, 1855.—CL. BERNARD, *Leç. de phys. exp.*, 1855.—GRIESINGER, *Arch. f. phys. Heilk.*, 1859, p. 48 ; 1862, p. 376.—PAVY, *On the Alleged Sugar-form. Funct. of the Liver*, 1861 ; *Res. on the Nat. and Treatm. of Diab.*, 1862.—SCHIFF, *Journ. de l'anat. et de phys.*, 1866.—SEEGEN, *Der Diab. mell.*, 1870.

Consult also the known text-books on physiological chemistry. Also : BOECKER, *Deutsche Kl.*, 1853, *No.* 33.—ROSENSTEIN, *Arch. Virch.*, 1857, XII., p. 414.—MOSLER, *Arch. d. V. f. wiss. Heilk.*, III.—THIERFELDER et UHLE, *Arch. f. phys. Heilk.*, 1858, p. 32.—HAUGHTON, *Dubl. Quart. J.*, 1861 and 1863.—REICH, *De diab. mell.*, Gryph., 1859.—GAEHTGENS, *Ueber den Stoffwechsel eines Diabetikers verglichen mit dem eines Gesunden*, Dorp., 1866.—HUPPERT, *Arch. d. Heilk.*, VII., p. 51 ; VIII., p. 331.—PETTENKOFER et. VOIT, *Sitzgsber. d. Münchn. Ac.*, 1865, II., p. 224 ; 1866, II.; *Ztschr. f. Biol.*, 1867, III., p. 381.—Also the literature on kidney diseases, etc., especially VOGEL.

MELLITURIA is usually a chronic, rarely an acute disease, in which, in consequence of an increased amount of sugar in the blood, of an almost constant increased amount of urine, of urea and of other ingredients of the urine, there is a smaller or larger amount of sugar (grape-sugar) excreted with the urine, and from which the patients usually die after progressive marasmus.

In the course of time many theories of diabetes have been propounded, which were partly founded upon ætiological and clinical grounds, partly upon physiological experiments. Most of these theories are insufficient to explain all the symptoms of the disorder. They can be divided into two groups : those which embrace all the phenomena of the disease, without regarding their immediate cause ; and those which endeavor to explain the cause of the disease.

I. (a) The theory first propounded by HUPPERT, and adopted by PETTENKOFER and VOIT, explains diabetes as a disturbance of nutrition, and ascribes the phenomena to an increased tendency to decay of the albuminous substances of the body. As the tissues of a diabetic patient are consumed much more rapidly than those of a healthy person, he has a proportionately greater want of food. As soon as he ceases to be

able to make good the loss of bodily substance by food, he must consume the bodily substance (the organ-albumen). This also explains the remarkable vulnerability of the tissues of diabetic persons (injuries healing very slowly) and their great prostration (they succumb to exertions and affections which healthy people could easily resist). This theory furthermore states that the mode of nutrition does not differ here from that of the healthy person : the albuminous substances are decomposed into nitrogenous compounds (urea) and into sugar. But as the formed blood-ingredients (the oxygen-carriers, partake of the quickened decay of the tissues, they are not capable, on account of their short existence, of carrying oxygen to the tissues in the same abundant quantity as in the healthy state. This explains why the diabetic does not absorb as much oxygen in proportion to the oxidizable substances contained in his blood, as the healthy person (but relatively less or absolutely as much as the healthy person in a state of starvation—PETTENKOFER and VOIT), and, furthermore, why it is that a smaller or greater portion of the sugar, formed from the albuminous substances, must be excreted in an unoxidized state (as such) : consequently the presence of sugar in the urine. The transformation of large quantities of albumen causes the greatly increased excretion of urea. The saturation of the tissues with the products of decomposition, especially with sugar, causes the thirst of the diabetics, and is perhaps also the cause of alterations of tissues (the decreased power of resistance). RANKE tends to believe that the increased quantity of sugar in the blood, similarly to a large amount of fat, influences the absorption of oxygen by the blood-corpuscles.

MEISSNER supposes that the decreased absorption of oxygen depends upon the fact that the diabetic excretes, unchanged, substances which in others contain oxygen, and that he therefore has a diminished need for oxygen ; but the blood of a diabetic is richer in sugar than that of a healthy person, and therefore it always contains in him more combustible material. This opposition to the theory is therefore disproved.

SCHULTZEN (Berl. kl. Wschr., 1872, No. 35) believes that in poisoning by phosphorus the blood loses in great part its capacity to oxidize, while the processes of fermentation continue. As after phosphorus-poisoning, by feeding on carbo-hydrates, the lactic acid (isomeric with glycerin-aldehyde which he discovered previously) increases, he believes that the latter compound should be accepted as the normal product of decomposition of sugar. In the diabetic this decomposition of the sugar does not take place on account of the disturbed action of fermentation, and it is excreted as such. But by giving 20–25 grm. of glycerin a day to the exclusion of all sugar-producing substances, the diabetic receives the actual combustible material, and S. consequently noticed disappearance of the sugar and of the symptoms of diabetes.

(b) The so-called gastro-intestinal theory presumes an excessive formation of sugar within the intestinal canal. The frequent beginning of the disease with digestive disturbances, moreover the intense thirst with want of appetite at first, and later the ravenous appetite ; the facts that the thirst is increased after the use of amylaceous substances, and that it is decreased by a meat diet,—speak in favor of this theory ; furthermore, the disappearance of the sugar in febrile diseases, in which the stomach and intestine are almost constantly affected ; etc. (ROLLO, BOUCHARDAT, M. GREGOR.) But this theory lacks any other important support, and these seemingly good reasons are disproved by the fact that if a diabetic starves, the disease still continues ; the sugar can therefore not be produced in the intestinal canal, but must be formed within the tissues.

(c) According to the so-called hepatic theory, the large quantity of sugar in the blood originates from the liver ; the diabetes would therefore only consist in an increase of a normal process, in an hypercrinia of the liver. This theory is mainly founded upon BERNARD's discovery, that the liver, independently of the food, even with pure meat-diet, produces glycogen (sugar of the liver), which is transformed into grape sugar by certain ferments ; as also upon the facts that diabetes cannot be induced in frogs whose liver has been extirpated ; that the diabetes induced in frogs by curare-poisoning disappears after extirpation of the liver (WINOGRADOFF), and lastly that diabetes cannot be induced, if the glycogenic function of the liver has been destroyed by chronic arsenical poisoning (SALKOWSKY, Med. Ctrbl., 1865, No. 49). But this power of the liver to change glycogen into sugar has become at the least doubtful by later physiological examinations ; besides, this theory is only founded upon several clinical and pathologico-anatomical facts which are just as consistent with the first-mentioned theory.

C. BOCK and F. A. HOFFMANN (Arch. f. Anat., Phys., u. s. w., 1871, p. 550) injected in a short period very large amounts of 1% solutions of chloride of sodium into

rabbits, and found in consequence first polyuria, in proportion to the amount of injected fluid, later mellituria. KÜNTZEL (*Exper. Beitr. z. Lehre v. d. Mellituria, Berl. Diss.*, 1872) found the same after injection of carbonate, phosphate, subsulphite of soda (1%), gum arabic, etc. ; he believes that the mellituria is only produced by mechanical means : through the disordered circulation the glycogen of the liver is brought into contact with the blood, and is changed by it into sugar. Compare with this KÜLZ (*Beitr. z. Hydrurie u. Mellituria*, Marburg, 1872).

(d) According to the pancreatic theory, the emulsioning and decomposition of the fats into fatty acids and glycerin cease in the different diseases of the pancreas (concretions within the duct, fatty degeneration, abscesses), so that the decomposed fat is prevented from entering the liver and there being used for the production of bile. In consequence thereof, the glycogen of the liver is changed into sugar, which is only partly consumed, the other part appearing in the urine. Cases of diabetes and pancreas diseases are related by BRIGHT, FRERICHS, BOUCHARDAT, MECKEL, SKODA, RECKLINGHAUSEN, KÜHNE and others. Also consult POPPER, *Oestr. Ztschr. f. pract. Heilk.*, 1868, No. 11. This theory is merely hypothetical, and is founded upon no facts whatever, excepting the above-mentioned clinical observations.

The three last-mentioned theories only try to explain the formation of sugar, which according to the first-mentioned theory is only an incidental phenomenon, and fail to discuss all other symptoms.

II. (a) The cerebral theory of diabetes is founded first upon the well-known experiments by BERNARD, according to which temporary diabetes (lasting several hours) can be produced in animals by a puncture of the floor of the fourth ventricle of the brain (between the origin of the *nn. vagi et acoustici*) ; then upon those cases in which dissection of diabetics showed a change of this portion of the brain (LEUDET, RECKLINGHAUSEN, LEVRAT-PERROTON, ZENKER, SEEGER, BÖTTCHER, and others), or of the cerebral vessels (RICHARDSON, MURRAY, BISCHOFF) ; then upon some ætiological conditions, as when diabetes suddenly occur after a concussion of the brain or of the whole body (ITZIGSOHN, PLAGGE and others), or after fright, passion, etc. ; further upon the diverse nervous affections accompanying the disease (hypochondriasis, insomnia, pains in different peripheral parts, paralyses, convulsions) ; lastly, perhaps upon the cure of the disease by some medicines (opium, quinia, arsenic), or by the galvanic current. But. these nervous diseases must not be attributed to a primary disorder of the brain. That diabetes is not identical with the glycosuria produced by puncture of the fourth ventricle, is proven by the fact that in one case the excretion of sugar is lasting, in the other only of short duration. But possibly the general disturbances of nutrition can be ascribed to the brain.

According to ECKHARDT (*Beitr. z. Anat. u. s. w.*, 1871, VI, 2. II.), hydruria of short duration, combined with diabetes, is produced by injury or irritation (mechanical or chemical) of the second lobe of the vermis of the cerebellum.

(b) The spinal theory of diabetes is founded upon the fact, that this state is produced not only temporarily, but also permanently, by the experimental destruction of the spinal cord for the length of one or two vertebræ in the inferior cervical or superior dorsal region ; as also because diabetes has been detected in man after fracture of the cervical portion of the spine.

(c) Diabetes has also been attributed to the *nervus splanchnicus :* after its section, GRÄFE, HENSEN, ECKHARDT and others noticed the occurrence of the disease. In nearly all of these cases congestive hyperæmia of the liver, according to SCHIFF paralysis of extensive portions of the vaso-motor nerves, forms the connecting link. It is stated that in the blood of these paralyzed vessels a ferment rapidly originates, which transforms the parenchyma of the liver into sugar. The sugar goes into the blood, and, after its quantity amounts to about 0.5%, into the urine.

According to SCHIFF. diabetes is also produced by the collateral hyperæmia of the liver after ligation of the *vasa afferentia* of both kidneys, also after section of the lumbar spinal cord or the sciatic nerves (in consequence of which paralysis of the vaso-motor nerves of the posterior extremities arises).

According to BERNARD, puncture of the medulla after previous division of the *nn. splanchnici* does not produce diabetes, but section of these nerves after puncture does not stop the existing diabetes.

According to CYON and ALADOFF (*B. de l'acad. imp. de Petersb.*, 1871, VIII., p. 91), the extirpation of the last cervical and the first dorsal ganglion, or of the former only, in dogs, induces diabetes (and vaso-motor paralysis of the anterior extremities). This depends upon the division of both *rami vertebrales*, or of the two nerves going to the *gangl. stellatum*, which encircle the subclavian artery. According to the two authors, antagonistic sets of fibres run within the lateral cords of the sympathetic, and in the

splanchnic nerves: some fibres come from the *ganglion stellatum*, and cause diabetes by their paralysis; the others originate deeper within the spinal cord and prevent the occurrence of diabetes by their paralysis. That this is in consequence of paralysis of the vaso-motor nerves, is proven by examination of the liver and hepatic artery. Diabetes produced by the authors was not accompanied by hydruria (that caused by puncture of the medulla always is).

F. A. HOFFMANN (*Arch. f. Anat., Phys. u. s. w.*, 1872, p. 746) produced diabetes in rabbits by subcutaneous injection of nitrite of amyl. (*Vide*, p. 165)

BRAUN (*Lehrb. d. Balneother.*, 1868, p. 343) noticed in four out of seven cases of sciatica $\frac{1}{2}$-$2\frac{1}{2}$ of sugar in the urine. SCHIFF noticed diabetes after compression or ligation of the main vessels of the extremities.

The SYMPTOMS OF DIABETES are explained partly by the presence of abnormally large amounts of sugar in the urine (thirst, polyuria, etc.), and by the saturation of the tissues with fluids containing sugar (muscular weakness, skin-diseases, etc.), partly by the fact that the consumption of matter in the body of the diabetic is considerably larger than in that of a healthy person, and that a large amount of nutritious material is excreted with the urine.

Usually there is very great appetite: in severe cases the diabetic eats two or three times as much as a healthy person could digest; at the same time he is constantly hungry and continues to emaciate. More remarkable still is the great thirst of the diabetic, especially after eating and at night. It is in consequence of the accumulation of the products of nutrition within the body (sugar, urea, etc.). (Occasionally there is not actual thirst, but only a sensation of uncomfortable dryness in the mouth.) The urine is consequently abundant (3–6, even 10 kil. a day), and its quantity is always greater than the quantity of the water imbibed (either in consequence of the water taken in the food, or the production of water in the organism). The quantity of sugar amounts on the average to 3–5% (250 grm. daily) even to 10% (.5 kil. daily). It is least before breakfast, most abundant after meals; the amount is greater, according to the starchy or sugary food taken, it is least with pure meat diet. But in the higher grades of the disease it is neither absent with a meat diet, nor if the patient be starved: it must therefore be produced from albumen (or fat). The quantity of urea is relatively smaller on account of the increased secretion of urine, but absolutely increased (two to three times greater than the normal), consequent upon the abundant nitrogenous food eaten. The uric acid is usually relatively increased.

All of the general ashy residue of the urine is excreted in absolutely larger, but also in relatively smaller amount.

That normal urine contains no sugar, see SEEGEN (*Arch. f. d. ges. Phys.*, 1872, V., p. 359), (*versus* BRÜCKE, B. JONES, KÜHNE, and others).

In regard to the excretion of uric acid in a case of diabetes, see KÜLZ (*Arch. f. Anat., Phys. u. wiss. Med.*, 1872, p. 293).

By what is above mentioned, the other characteristics of the urine are explained: it is usually pale, rarely dark, often cloudy, slightly foamy, of a weak acid reaction, of a musty odor, of a sweetish taste, somewhat sticky. Its specific gravity varies from 1025 to 1040 (it rarely varies more). In the later stages the urine is usually albuminous.

The amount of sugar in the urine is no criterion of the state of the disease: for the quantity of sugar is usually due in great part to the carbo-hydrates of the food; the body (the decomposed organ-albumen) produces but a small amount. The fat produced from the albumen seems to be further transformed in the diabetic into sugar,

while the fat, existing as such, is always decomposed into carbonic acid and water (PETTENKOFER and VOIT).

Besides the urine, most of the other se- and excretions contain sugar, occasionally perhaps alternatingly with the urine: it is present in the usually relatively spare, dry, more rarely diarrhœal fæces; the saliva; the occasionally profuse perspiration.

The diabetic does not absorb, notwithstanding the increased transformation of matter, more oxygen than a healthy person. In consequence of this relatively small absorption of oxygen by the diabetic, the excretion of carbonic acid by the skin and lungs is not only not in proportion to the total nutrition, but less than a healthy person would excrete with an equally large amount of nourishment, because a smaller or larger portion of combustible matter (sugar) is excreted unchanged. Hydrogen gas and marsh gas have rarely been found in the products of respiration. Just like a larger proportion of the total carbon which takes part in the process of nutrition, so more water passes off by the urine and correspondingly less by the skin and lungs: in larger quantity by the urine, because it is carried along by the products of decomposition as their dissolving menstruum. The excretion of nitrogen in the diabetic is in severe cases greater than the quantity of nitrogen contained in the food: the diabetic therefore loses organalbumen.

Therefore the diabetic, notwithstanding the abundant imbibition of nourishment, finally can no longer sustain his organs in a normal state of nutrition: emaciation and a series of marasmic conditions set in, which ultimately produce death. Most of them are similar to those of inanition (see p. 527). The following symptoms arise in some cases, some of which, just like the increased amount of urine, the sugar in the urine, the intense appetite and thirst, first direct the attention to the diagnosis of the disease.

The emaciation involves the tissues and organs in a mode similar to that of inanition; the skin becomes thinner, its epithelium is reproduced in a decreased measure; its glands are less active; the skin of the diabetic is usually dry, cracked, generally not perspiring; the latter certainly in consequence of the abundant loss of water through the kidneys. (Occasionally the exhalation from the skin has a disagreeable odor.) In some cases pruritis exists. The loss of hair must also be mentioned here.

The insensible perspiration is very much diminished (to about half) in *diabetes mellitus* and *insipidus*. BÜRGER (*D. Arch. f. klin. Med.*, 1873, XI., p. 323).

The adipose tissue disappears from the external and internal parts of the body: the diabetics attain an equally excessive degree of emaciation as the subjects of starvation, even while they partake so largely of nourishment. This is most noticeable if the disease occur in a very stout person.

The entire muscular system undergoes atrophy: the emaciation of the muscles explains the ready fatigue and debility of the diabetic. The pulse is usually small, though of normal frequency.

The diminished muscular strength may be due either to the fact that in consequence of an increased excretion of sugar and a diminished absorption of oxygen the main source of muscular activity is lost; or (?) that the products of decomposition in the blood of a diabetic decrease the muscular excitability (as, according to RANKE, lactic acid).

Emaciation of the heart, atrophy of the muscles of the stomach and intes-

tines, etc., increase the tendency to the occurrence of disordered nutrition.

Atrophy of the glandular organs of the mouth and throat, of the stomach and intestine, the salivary glands and those of the pancreas, occasionally also of the liver, all of which are sometimes present simultaneously and to the same extent, sometimes only in the last-named organs, also influence the diminished nutrition and tissue-formation, notwithstanding the abundant nourishment. Atrophy of the genital organs occasions in men impotence, in women at least partial amenorrhœa and sterility. But impotence and sterility are also often present in still vigorous diabetics.

Similar atrophy occurs in the bones and teeth. The latter become loosened and frequently carious, certainly usually with an acid, although occasionally with an alkaline reaction of the saliva.

The central nervous system only becomes atrophied at a later period and in a less characteristic degree. But especially the sense of sight shows quite frequently disorders which can for the greater part be attributed to its atrophy or to the atrophy of some of its parts: disorders of the accommodation without demonstrable changes in the affected parts, atrophy of the retina; but especially production of cataract.

The temperature of the body is occasionally normal, occasionally diminished, naturally increased if any inflammatory complications exist.

The organs of digestion show no characteristic abnormality: the not rarely occurring disorders of the tongue, stomach, and intestines are all explained by the large quantity of food taken. In proportion to this the digestive power is quite good.

The permanently impaired nutritive condition of diabetics explains, at least partly, their great vulnerability, their tendency to inflammations terminating in suppuration and not rarely in gangrene, and the frequent occurrence of so-called tuberculosis.

The ready vulnerability of diabetics is especially noticeable by the skin: wounds of all kinds, from operations, from venesection, also of the eyes (from cataract operations) heal with difficulty, rarely by first intention, usually with suppuration, or even gangrene sets in; at the orifice of the urethra balanitis frequently occur, favored by the decomposition of stagnant urine, in women superficial inflammations of the vulva; occasionally for months furuncles and carbuncles form, or more extensive cellular tissue inflammations with tendency to gangrene; even gangrene of the toes similar to *gangrena senilis*.

Of the inflammations of the mucous membranes those of the oral cavity, frequently of a scorbutic character, and of the air-passages with consecutive lobular, frequently tuberculous pneumonias, are especially deserving of observation. The greater number of diabetics, especially of the lower classes, die of so-called pulmonary tuberculosis; more rarely from gangrene of the lungs.

SEEGEN describes several peculiarities of the tongue of diabetics, whose cause is unknown.

The kidneys present, besides hyperæmia and perhaps hypertrophy, which are the consequences of their increased function, frequently the characteristics of *morbus Brightii*.

The INVASION of diabetes is usually gradual, rarely rapid or sudden.

The DURATION of diabetes is on the average from one to three years, rarely less, occasionally five to ten, even fifteen to twenty-five years. Whether

those cases of quite acute diabetes, of a few days' or weeks' duration with termination in health, are identical with the usual form, is questionable. The latter has been observed during some cerebral and hepatic diseases, in carbonic oxide poisoning, in poisoning by curare, corrosive sublimate, after inhalation of ether and chloroform, etc., in extensive burning, after varnishing the skin.

Many observations of glycosuria of this kind date from a time when grave errors were liable to be made in regard to the detection of sugar in the urine; in many such cases the urine probably contained no sugar whatever.

Its COURSE is in the main quite regular, excepting when great changes are made in the diet, or if intercurring acute affections arise. Rarely it is irregularly intermittent. Many patients are by absolute abstinence of amylaceous food in perfect subjective health; in some even the glycosuria disappears during this time.

Some make a distinction of two stages of the disease, which SEEGEN believes to be two different forms. The patients with the first form only excrete sugar with the urine when they partake of saccharine or amylaceous food; if not, all excretion of sugar and every symptom of diabetes disappears. The patients afflicted with the second form of the disease also excrete sugar, even if they have an exclusive meat diet; ingestion of nutriment containing sugar, etc., increases in them the excretion of sugar and the symptoms of diabetes. The course of the disease in patients of the latter class is more rapid, especially if the patients are young, if they have not a sufficient meat-diet, and if the disease is hereditary.

The TERMINATION of chronic diabetes in health is extremely rare. Usually death occurs: most frequently from chronic phthisis of the lungs alone or simultaneously with other organs, more rarely from simple marasmus, albuminuria, carbuncle, etc.; by suicide.

The ÆTIOLOGY of diabetes is in the main still unsettled. It appears most frequently in the bloom of life, more frequently in male subjects, proportionately frequently in obesity. Not a few of the cases are hereditary: injuries (*vide supra*), colds, malarial poisoning, continuous excessive exertions, depression of the mind, habitual use of amylaceous or saccharine substances, cakes, etc. (*i.e.*, bad nourishment), working in sugar refineries (?), previous severe diseases. In most cases a particular cause cannot be found.

In regard to diabetes mellitus in children, see SENATOR (*Berl. klin. Wschr.*, 1872, No. 48).

SEEGEN accepts still another form of diabetes (?), which occurs in consequence of sexual excesses, especially of onanism. The urine usually only contains several tenths per cent. of sugar. Polyuria is absent, but there exists a frequent desire for micturition.

Diabetes, usually of no importance and of short duration, occurs, according to some, in the defervescence of diverse febrile diseases (measles, pneumonia, etc.).

PATHOLOGICAL ANATOMY has not yet demonstrated a constant state of the body in diabetes. Usually emaciation is excessive; in a large majority of the cases tuberculosis of the lungs is found, usually in the form of tuberculous pneumonia; the liver is usually hyperæmic; usually chronic catarrh of the stomach exists; frequently hyperæmia, hypertrophy, and parenchymatous inflammation of the kidneys; rarely atrophy of the pancreas.

[Consult W. H. DICKINSON, On Certain Morbid Changes in the Nervous System, associated with Diabetes. *Med.-Chir. Trans.*, LIII., p. 233, 1870.—ED.]

DIABETES INSIPIDUS, POLYURIA.

R. Willis, *Dis. of the Urin. Syst.*—Neuffer, *Ueb. Diab. ins.*, 1856.—Leyden, *Berl. klin. Wschr.*, 1865, No. 37.—Strauss, *Die einf. Zuckerlose Harnruhr*, 1870.—Ebstein, *D. Arch. f. klin. Med.*, 1873, XI., p. 344.—Trousseau, *Clin. Méd.*, II., p. 699, 1865.

Diabetes insipidus is an occasionally acute, usually chronic disease, in which, just as in diabetes mellitus, there is an abundant excretion (five to fifteen kil. in twenty-four hours) of urine, not containing sugar, but containing a large amount of solid ingredients (specific gravity 1004–1012).

If the disease be acute, as in convalescence from divers acute disorders, or in consequence of a spontaneous strong diuresis, or one produced by medication, or if it is only of occasional recurrence, as in some cases of hysteria, etc., it is of no great general importance, and is almost always curable.

If the disease, on the contrary, be chronic, the same symptoms as in diabetes mellitus are present : excessive thirst, emaciation, debility, pains in the head and limbs, dyspeptic phenomena, obstinate constipation. In some cases there are also psychopathy, epilepsy, etc. A cure is rare. Death usually only occurs from intercurrent diseases.

The disease occasionally arises suddenly, sometimes gradually ; most frequently it attacks young people.

The affection causing simple chronic polyuria is most probably located in the brain : in favor of this is the physiological experiment of injuring a certain point in the floor of the fourth ventricle, in consequence of which an increased secretion of urine, lasting several days, occurs ; and also clinical observation. In several lately reported cases polyuria had occurred in consequence of violent encephalopathies, due to constitutional syphilis, and disappeared under appropriate treatment. In other cases dissection proved different disorders of the brain, more particularly the medulla oblongata.

The cases in question are cited by Jaksch, Luys and Dumontpallier, the Author, Leyden, Mosler, Fernet, Gentilhomme, Lancereaux, Pribram, Ebstein.

The mode of origin of *diabetes insipidus* is not known. According to Pettenkofer and Voit, albumen and fat are perhaps decomposed in large quantities, just as in mellituria, and not enough is introduced into the body to make good the loss, but everything is consumed to carbonic acid and water : if that were true, *d. insipidus* would only differ from *d. mellitus* by the absence of sugar in the urine.

According to Pribram (*Prag. Vjschr.*, 1871, IV., p. 1), the increased excretion of urea in diabetes insipidus is secondary. Under certain circumstances the polydipsia is primary.

DIABETES INOSITUS.

This is that form of diabetes mellitus in which inosite, a non-fermentable sugar contained in the muscles, takes the place entirely, or at least preponderatingly, of the grape sugar. Minute quantities of inosite have been found frequently in the urine in diabetes as well as in other diseases (albuminuria, etc.).

Vohl, *Arch. f. phys. Heilk.*, 1858, p. 410.

XV. PYÆMIA (SEPTICO-PYÆMIA).

(Pus-poisoning. Purulent fermentation of the blood. Metastatic dys-

crasia.   Purulent diathesis.—Septicæmia.   Ichorrhæmia.   Putrid infec-
tion.)

J. HUNTER, *Transact of the Soc. for the Impr. of Med. and Chir. Knowl.*, 1793, V.,
1.—GASPARD, *Journ. de phys. par Magendie*, 1822, II., p. 1 ; 1824, IV., p. 1.—MA-
GENDIE, *Journ. de phys.*, III., p. 81 ; *L'union méd., Jan., Oct.*, 1852.—CRUVEILHIER,
Rev. méd., 1826 ; *Dict. de méd. et de chir. prat., art. Phlébite.*—BAYLE, *Mém. sur la
fièvre putr. et gangréneuse, Rec. méd.*, 1826, II., p. 89.—DANCE, *Arch. gén. de méd.*,
1828, p. 473 ; 1829, pp. 5 and 161.—ARNOTT, *Med.-Chir. Transact.*, XV.; *Path.
Unters. d. secund. Wirk. d. Venenentz, Uebers.*, 1830.—TESSIER, *Rec. de méd. vétér.
prat.*, 1839 ; *Arch. de méd.*, t. III.—D'ARCET, *Rech. sur les abscès multiples et sur
les accidents, qu'amène la présence du pus dans le syst. vasc.*, 1842.—BÉRARD, *Dict. de
méd.*, 1842., XXVII.—LEBERT, *Phys. path.*, 1845.—CASTELNAU et DUCREST, *Mém.
de l'acad.*, 1846, XII.—VIRCHOW, *Med. Reform.*, 1848, No. 15 ; *Ges. Abh.*, 1856, p. 219,
p. 636, etc.—SÉDILLOT, *De l'infection purulente ou pyoémie*, 1849.—SIMPSON, *Edinb.
Monthly Journ., Nov.*, 1850.—BECK, *Unters. u. Stud. im Geb. d. Anat., etc.*, 1852.—
MAISONNEUVE, *Mém. de la soc. de chir.*, 1853 ; *Compt.-rend.*, 1866, LXIII.—STICH,
Ann. d. Char.-Krank., 1853, III., p. 192.—THIERSCH, *Infectionsverss. an Thieren
etc.*, 1854.—GOSSELIN, *Mém. de la soc. de chir.*, 1855, V., p. 147.—PANUM, *Bibl. für
Laeger.*, 1856, VIII., p. 253 ; *Schmidt's Jahrb.*, 1859 ; *Virch. Arch.*, XXV., p. 441.—
ROSER, *Arch. de Heilk.*, 1860, I., p. 39 *et seq.*—WYSS, *Beob. üb. Septikämie, Zürich Diss.*,
1862.—BILLROTH, *Arch. f. klin. Chir.*, 1862, II., p. 325 ; 1864, VI., p. 382 ; 1865, VI.,
p. 372 ; 1867, IX., p. 52.—KIRKES, *Brit. Med. Journ.*, 1863, No. 149.—O. WEBER,
Deutsche Klin., 1863, No. 48 ff. ; 1864, No. 1 ; 1864, No. 48 ; 1865, No. 2.—WAGNER,
Arch. d. Heilk., 1865, VI., p. 146, p. 369, p. 481.—SCHWENINGER, *Ueb. d. Wirk.
faul. Subst., etc.*, 1866.—HEMMER, *Exper. Stud. üb. d. Wirk. faul. Stoffe, etc.*, 1866.—
WALDEYER, *Virch. Arch.*, 1867, XL., p. 379.—SCHMITZ, *Zur Lehre vom putriden
Gift., Dorp. Diss.*, 1867.—LISTER, *Brit. Med. Journ.*, 1867, No. 351.—BERGMANN,
Petersb. med. Ztschr., 1868, XV., p. 16.—HUETER, *In Pitha-Billroth's Hdb. d. Chir.*,
I., 2. *Abth.*, p. 1, 1869.—FISCHER, *Ueb. d. heut. Stand d. Forsch. in d. Pyämielehre*,
1869.—The latest literature is indicated *infra.*

The literature on puerperal fever is very voluminous.   Those who described it first
were PEU, VESOU, WILLIS (1682), who introduced the name of "*febris puerperarum*,"
DE LA MOTTE and MALOUIN (1746).   Its essential nature was insisted upon particu-
larly by KIWISCH and LITZMANN.   The greatest credit for the demonstration of the
contagiousness of this disease is due to SEMMELWEISS (*Die Ætiol., der Begriff. u. die
Prophyl. des Kindbettfrs.*, 1861).   Also save VEIT (*Krankh. d. weibl. Geschlechtsorgg.,
In Virch. Handb. d. spec. Path. u. Ther.*, 1867).

PYÆMIA, SEPTICO-PYÆMIA, is usually an acute disease, starting in a puru-
lent or ichorous focus situated on the external surface of, or within the
body, caused by the absorption of mechanically or chemically noxious, so-
called septic or putrid substances, which originate in that focus and in its
vicinity, and which is characterized by symptoms of a severe febrile consti-
tutional disorder, usually with prominent nervous symptoms, frequently by
simultaneous venous thrombosis with emboli, by chills and by so-called
metastatic abscesses in diverse organs, especially the lungs, with inflamma-
tion of their serous membranes.

The usual cases of surgical pyæmia and of puerperal fever are composed
of mechanical or chemical processes.   They consist of embolic inflamma-
tions, which have their starting-point usually in the veins of the injured
part (so-called embolic pyæmia), and of a constitutional disorder, which is
the consequence of the absorption of noxious fluid or gaseous, or, according
to later examinations, vegetable substances (globular bacteria), formed at
the wound or propagating there (so-called septicæmia, septic pyæmia).   Clin-
ically the two processes cannot always be separated : frequently the coarse
emboli are at the same time impregnated with the noxious substance, so
that the mechanical and chemical injurious effects appear simultaneously at
the place of deposition of the emboli.   But, as cases of septicæmia also
occur by themselves, without thrombosis and without consecutive embolic

inflammation; while, on the other hand, thrombi and emboli, acting merely mechanically, never produce pyæmia, we must place septicæmia in the foreground, and make it the basis of observation.

The difference between septic and embolic pyæmia was first distinctly defined by GASPARD, and in Germany by VIRCHOW.

I. SEPTICÆMIA OR ICHORRHÆMIA.

(Septic or septicæmic or ichorræmic pyæmia. Traumatic sepsis. Putrid infection.)

The causes of septicæmia are extensive and severe (causing gangrene) contusions of soft parts and of bones, usually with, more rarely without injuries of the skin; injuries and non-traumatic affections of every kind, in the course of which decompositions of the extravasated blood, of stagnant pus, of gangrenous tissues occur (diverse affections of the bones, especially acute periostitis and osteo-myelitis, skull-injuries, puerperal diseases, so-called cold or lymphatic abscesses, in which the disease appears usually only secondarily, after spontaneous and particularly after artificial opening). Probably also some forms of gangrene partly belong here (bed-sores, scorbutic gangrene, gangrene from fæcal and urinary infiltration), as also poisoning from dissection-wounds, so-called pseudo-erysipelas of the subcutaneous, intermuscular, etc., tissues, some inflammations of the cellular tissue and in the neighborhood of the salivary glands, and the severe so-called diphtheritic inflammations of the throat and the large intestines.

Some also include in this class common traumatic fever, inasmuch as in every wound, which does not heal by first intention, some of the tissues die; also the so-called surgical after-fever, which occurs later than traumatic fever and which usually is the consequence of retained pus, as also of slight inflammation of the subcutaneous and intermuscular tissue; lastly, the so-called milk-fever after confinement (HALBERTSMA, *Med. Ctrlbl.*, 1870, No. 25). Perhaps also the so-called secondary or purulent fever in the stage of suppuration or maturation of small-pox belongs here. But it is at present hardly justifiable to enumerate with the above several other acute non-surgical diseases, which are characterized particularly by their unknown origin, their rapid course accompanied by serious fever and nervous symptoms, their not infrequent termination in death, and by the insufficient facts discovered in *post mortem* examinations (the various typhoid conditions, yellow fever, scarlatina, etc.).

Several diseases, which arise in consequence of partaking of decomposing food and drink, and respiring the air of illy-ventilated dead-houses and hospitals (so-called hospital catarrh of the stomach and intestines), partly belong here.

According to the position of the centre of the septic poison within or without the body of the patient, HUETER makes a distinction of autochthonous and heterochthonous septicæmia.

Many make a distinction between septicæmia and ichorrhæmia. The decomposition is said to originate spontaneously in the latter, and in consequence of an extraneous agent in the former.

Septicæmia (putrid infection) originates through putrefying and decaying substances, which get (accidentally or—in experiments—purposely) into the blood; ichorrhæmia (ichorrhæmic infection) is produced by a substance not at present more closely definable (VIRCHOW's *ichor*), which is formed within the body in some diffused purulent discharges without any actual gangrene. Anatomically and clinically septicæmia and ichorrhæmia are inseparable. But it must not be understood that this proves the identity of both processes, nor that the one or the other is a strictly scientific conception. Both are only generic terms for probably very differ-

ent conditions, whose chemical character is still very little known to us, but which display to our present knowledge certain pathologico-anatomical and especially clinical analogies.

The PATHOLOGICAL ANATOMY of septicæmia (as well according to experiments as to observations in man) is not very characteristic. If the origin of the disease is of a traumatic nature, non-circumscribed, but diffused, bloody or ichorous infiltrations, varying in extent and depth, appear. But almost constantly present are only incomplete coagulation, and diminished consistency of the blood, usually acute enlargement and softening of the spleen; occasionally (in animals almost constantly) acute intestinal catarrh with enlargement of the intestinal follicles and mesenteric glands, often slight hæmorrhages of the serous and mucous membranes, occasionally enlargement of the liver and kidneys. The brain, etc., show no characteristic conditions. Nowhere are there any metastatic abscesses. The corpse putrefies very rapidly.

The SYMPTOMS of septicæmia appear usually 2–4 days after the injury, in non-surgical cases at an uncertain period after the commencement of the disease. The wound often does not at all suppurate, but discharges a thin bloody or ichorous secretion, occasionally containing air-bubbles; in its vicinity, occasionally very extensive, inflammatory œdema develops within a few hours or days; so-called *gangrène foudroyante*, acute purulent œdema, progressive gangrene of the cellular tissue. The skin is of a peculiar reddish-brown color. The actual constitutional disease mostly begins quickly, usually without, more rarely with chills. Rarely the disease is unattended by fever. Nearly always severe, continuous or light remittent fever (temp. 39°–40° C.) exists, occasionally after a previous fall of temperature. The pulse is frequent, commonly small; the respirations are increased. Almost always intense thirst, dry tongue, and want of appetite exist. The sensorium is influenced, as in serious typhoid cases, so that existing, at other times painful affections are painless. Usually quiet delirium, more rarely restlessness, is present. Occasionally, slight icterus, mostly without icteric condition of the urine, occurs. Rarely, abundant diarrhœa sets in, occasionally with all the symptoms of cholera. The skin at first frequently perspires abundantly, later it is usually dry; the urine is scanty, dark, occasionally albuminous. All movements are feeble. Death occurs, frequently with agony of long duration, sometimes after a few days, usually at the end of the first week.

Here perhaps belong also many cases of puerperal fever, which terminate fatally after a course of a few days or weeks, mostly soon after the confinement, even already previous to it, which begin with chills, and run through their course with nervous symptoms, high fever and quickened respiration. Dissection shows negative results, or the appearances above stated.

In very rare cases death occurs after chronic suppuration of long duration, without the occurrence of metastatic foci as shown by dissection : so-called traumatic hectic, traumatic phthisis, pyæmic marasmus. Many accept this as a chronic septicæmia.

2. EMBOLIC PYÆMIA, PYÆMIA IN ITS RESTRICTED MEANING, SEPTICO-PYÆMIA.

The CAUSES of embolic pyæmia are most frequently so-called compound fractures, severe contusions of the soft parts, extensive amputations and resections (more rarely surgical operations which only implicate the soft parts), traumatic and non-traumatic suppurating periostitis and osteo-myelitis, suppurating phlebitis, puerperal endometritis, rarely suppurations of

the internal organs, most frequently those of the urinary passages, the large intestines, and the heart. Pyæmia occurs sporadically, as well as epidemically and endemically, under such circumstances even in relatively light injuries, or primary affections. It causes the large majority of fatal cases after severe operations, especially amputations, in hospitals, and the large mortality in lying-in hospitals in proportion to that in private practice. In all these cases there are either no demonstrable causes ; or they are noxious substances, which are contained in unclean hands, instruments, bandages, sponges, beds, etc. ; or in the air of those localities in question (overcrowded or badly ventilated sick-houses and lying-in wards). A so-called primary or spontaneous pyæmia is not demonstrated.

ANATOMICALLY it is especially characteristic, that embolic pyæmia has its source in a venous thrombosis. Consequently it occurs most frequently where dense and extensive venous plexuses exist, e.g., in the hæmorrhoidal and uterine veins, as also where the injured veins cannot reunite for physiological reasons (veins of the bones), or on account of preceding diseases (formation of cicatrices in the vicinity), or in consequence of badly-applied bandages, etc.

Thrombosis of veins occurs most frequently in the larger or medium-sized vessels, which run at the point of the primary wound, or at least communicate with it (so-called traumatic, compression, and inflammatory thromboses) ; more rarely in those which are not in direct communication with it (e.g., in injuries of the extremities, in the veins of distant large muscles, in those of the vertebral region, of the pelvis : so-called dilatation- and marantic-thromboses). In both cases the production of venous thromboses is favored by weakened activity of the heart, but also partly by unknown circumstances (dyscrasia, or more ready coagulability of the blood in the wounded ?).

PETIT (*Gaz. hebd.*, 1871, No. 31) calls attention particularly to the smaller inter- and intra-muscular veins, which lie in the immediate site of the operation-wound, or in its vicinity.

The thrombi in the parts in question do not organize, but they undergo a simple, more frequently a putrescent softening. The latter is produced or at least favored by ichorous suppuration in the parts surrounding the veins containing the thrombi : the ichorous poison is diffusible.

The thrombi of the veins in pyæmia are situated occasionally in unchanged vessel-walls, occasionally the latter are infiltrated with pus or ichor in one or in all of their tissues, the internal as well as the external, the connective tissue coat (suppurating and septic phlebitis) ; primary and secondary thromboses.

Emboli produced from such thrombi go from the right heart into the lungs ; by preference first into the posterior parts of the inferior lobes (see p. 201), where they can be demonstrated in almost every case. They very rarely remain impacted in larger, most frequently in medium-sized and small arterial branches, or even in capillaries. Here they cause rarely only hæmorrhagic infarcti, usually metastatic abscesses : the latter, because they are usually in a state of ichorous decay, and cause a similar decomposition of the products of inflammation in the coats of the vessel (pulmonary artery) and its surrounding parts. In their vicinity the lung-tissue is hyperæmic and œdematous, or hyperæmic and hæmorrhagic, or merely in a state of catarrhal inflammation. The number of these centres is variable, in general so much the greater the oftener the patient has had chills.

In a large majority of cases infarcti and abscesses only occur in the lungs, while in others they are also present in the spleen, kidneys, and liver, and still in other (almost in all) of the vascular organs.   The suppurating or putrid emboli, which are the causes of those infarcti and abscesses, get into these organs either after they have passed through the lungs; or the thrombi of the pulmonary artery pass into the pulmonary veins and their thrombi form emboli; rarely the emboli are carried directly by means of a sort of reversed current into the different organs (e.g., those from the inferior branches of the vena portæ into the veins of the liver; see p. 201).

In a careful examination of the bodies of pyæmics thrombi are frequently found, besides venous thrombi which are imbedded in ichorous surroundings, whose adjacent parts are in this respect normal.   Such thrombi sometimes do not occasion, if they form emboli, metastatic abscesses; at other times these do originate, probably because the thrombi become infected by altered blood on their way from the periphery to the lungs.   Lastly, some coagulations in the lungs are secondary, only arising in consequence of the formation of infarcti.

Experiments in regard to this (the action of bodies obstructing vessels and the production of multiple abscesses by them) were first made by CRUVEILHIER, later especially by VIRCHOW.   The close relation of venous thromboses and venous inflammations to pyæmia was insisted upon already by BICHAT and HODGSON, later by SASSE, BOUILLAUD, CRISP, CARSWELL, GULLIVER, CRUVEILHIER, ROKITANSKY, DANCE, and ARNOTT.

Though the origin of metastatic deposits in the lungs is explained, that of those in other organs is still doubtful.   In cases where the lungs are free from such deposits, it can be supposed that several small coagula, of about the size of white blood-corpuscles, pass through the lung capillaries, and, enlarging by deposits of fibrin from the blood, become impacted in the capillaries of other organs; or that larger coagula pass accidentally through such parts of the lungs where direct changes of arterial to venous branches exist.   Where metastatic deposits are found in the lungs and other organs simultaneously, the same mode of origin may be accepted, or the deposits in the kidneys, etc., may be believed to be the products of transported secondary coagula, that is coagula passed from the pulmonary artery through the capillaries into the branches of the pulmonary veins.

The serous membranes, to whose surface the abscesses extend, especially the pleura, present circumscribed or diffused inflammations, frequently with suppurative or ichorous exudation.   More rarely such inflammations of the serous membranes exist without demonstrable abscesses of the organs in question, occasionally there are similar inflammations of the joints.   Their origin is not yet known.

The lymphatic vessels starting from the primary purulent focus are frequently normal, rarely more abundantly filled with the usual lymph or that made cloudy by an admixture of pus.   Their lymphatic glands are usually more or less hyperæmic and swollen, in a state of cellular hypertrophy. The other lymphatic glands are nearly always normal, more rarely they are similarly affected, but in a lesser degree.   The spleen is commonly more or less hyperæmic and swollen by the same hypertrophy.   The blood is richer in colorless corpuscles and contains globular bacteria (vide infra).   Its chemical examination has not as yet shown anything.

The other organs show the same changes as after other serious febrile diseases which cause acute marasmus.   The liver often presents parenchymatous infiltration.   The occasional icterus is usually not of mechanical nature (see p. 556).   The kidneys are similarly changed as the liver.   The stomach and intestines are occasionally in the same condition as in septicæmia.

The SYMPTOMS OF PYÆMIA are in the majority of cases characteristic. They usually set in suddenly.   Almost always moderate or high fever exists:

38°–41° C.; pulse 120–140, at first large, full, even dicrotic, later small, soft; increased respirations. The temperature sinks from this height frequently in a few hours to its normal degree. The affection begins most frequently with a severe chill, lasting several minutes to one hour and more, with a temperature of from 40° C. to almost 42° C., which is attained occasionally in a few hours; the chills recur during the first days usually daily, rarely regularly, at times even several times a day, less frequently they are entirely absent; consequently to the chill a sensation of intense heat, and profuse perspiration sets in. The skin is either dry or damp, occasionally covered with sudamina; later it becomes frequently more or less icteric. There are loss of appetite, great thirst, thickly coated, frequently dry tongue; not rarely painless diarrhœa: the face is haggard; general bodily and mental depression; frequently headache; often moderate enlargement of the spleen. Later on only moderate symptoms on the part of those organs which are affected by the metastatic inflammations, appear: most frequently symptoms due to the respiratory organs and pains in the joints; though the latter are often, notwithstanding intense inflammation, quite painless. Rarely are characteristic symptoms of the other affected organs present. Quite frequently bed-sores exist. The external wound, which has caused pyæmia, very rarely shows no changes. Nearly always they do occur, sometimes even before, more frequently only after the first chill. If the wound be lately made, neither *prima intentio* nor suppuration occurs, but a rapid decay of the injured tissues and an unusually intense inflammation of the surrounding parts (intense hyperæmia, great œdema, etc.), sometimes with a similar affection of the vascular and lymphatic vessels (including the lymphatic glands), or without. If the wound has already commenced to granulate, its secretion usually diminishes, so that its surface appears as though it were varnished; or the previously yellow, cream-like pus becomes yellowish-green, thinner, ichorous; or the wound bleeds. The wound itself looks inflamed, and is painful; existing granulations become smaller and more flabby; the already commenced healing stops. The parts surrounding the wound are œdematous, or evenly or irregularly flushed; the entire limb occasionally appears remarkably withered. The veins and lymphatic vessels give more or less distinct signs of thrombosis and inflammation. Nothing is known in regard to the changes of the primary purulent centre, if it is not upon the external surface of the body.

After an usually acute course, lasting one to two weeks, more rarely a sub-acute and still more rarely a chronic course, in which the chills decrease in number and intensity, death occurs, rarely convalescence. The latter is observed in private practice more frequently than is usually thought.

In regard to the condition of the temperature, see WUNDERLICH, *Das Verh. d. Eigenwärme*, 1870, p. 344; HEUBNER, *Arch. d. Heilk.*, IX., p. 289; SEGUIN's *Thermometry*, 1876, pp. 156, 161.

Pyæmia does not in all cases show either of the above-described sets of symptoms. In some cases (in consequence of insufficient absorption of the noxious substance ?— or in those less disposed ?) it occurs only in the form of a so-called pyæmic febricula (MALGAIGNE, STROMEYER, ROSER) in women after confinement as so-called milk-fever. At other times it occurs as so-called traumatic or pyæmic erysipelas, or as pyæmic diarrhœa (ROSER). Still in other cases slow suppuration is developed, without fever and without any great constitutional disturbance in the skin in several joints.

Is an affection ætiologically, anatomically, and symptomatically similar
to pyæmia in general, sometimes more to its septicæmic, sometimes more to
its embolic form; only differing from it by the affected individuals. It
occurs in the largest majority of cases in women after parturition, but is
also found in exactly the same form in pregnant women, in their children,
in non-pregnant women, in women upon whose genitals operations have
been performed.

Just as ordinary pyæmia, puerperal fever occurs rarely sporadically,
most frequently epidemically and endemically.

The affections of the puerperal state which occasion pyæmia are : puer-
peral endometritis and endocolpitis of a catarrhal, so-called croupons or
diphtheritic nature : colpitis is most frequently preceded by lacerations of
the vulval orifice, produced by the child-birth, or by parenchymatous
hæmorrhages, which are transformed into simple or ichorous ulcers ; endo-
metritis is frequently due to lacerations of the *cervix uteri ;* diffused metri-
tis, and diffused or circumscribed parametritis (so-called extra-peritonæal
pelvic abscesses) : the former two forms occur alone, or are combined with
lymphangioïtis or with other puerperal inflammations ; diffused metritis
originates most frequently in lacerations of the vagina, more rarely from
contusions of the cervix ; puerperal thromboses, particularly of the uterus
and its appendages : originating primarily, as well as after metritis, etc. ;
perimetritis, which originates directly from an endometritis, metritis, and
parametritis, or from a salpyngitis ; suppurative peritonitis.

Each one of the above-named affections may become the cause of puer-
peral fever : most frequently it is diffused metritis and endometritis, whence,
by means of the veins or lymphatic vessels, or both, the general circulation
receives noxious substances. These different affections are almost never
found simultaneously and irregularly in the same epidemic or endemic,
but almost always one of them predominates. This has rightly led to the
acceptation of so-called forms of puerperal fever. These diversities are mostly
present in those affections which are secondary to the above-mentioned
principal affections (secondary parotitis, puerperal scarlatina, etc.). Finally,
they also influence the mortality in different epidemics : dissection occa-
sionally shows remarkably numerous, occasionally very slight local lesions.

According to BUHL (*Mon.-Schr. f. Geburtsk. u. s. w.*, 1864, XXIII., p 303). non-
puerperal traumatic interferences with the vagina and uterus (*e.g.*, episiorrhaphy,
écrasement of an epithelial cancer of the vagina) may also produce a disease similar
in every respect to puerperal fever : diphtheria and gangrene of the surface of the
wound. suppurating lymphangioïtis in the sub-peritoneal connective tissue of the
uterus, suppurating peritonitis and frequently also pleurisy. The puerperal fever
loses thereby everything specific : it is only a pyæmia originating from the genitals.
Only the form of the injury, here an operation, there preceding parturition with usual
or unusual consequences, makes the distinction.

Suppurating peritonitis can cause pyæmia by the pus entering the blood through
the lymphatic vessels of the diaphragm, and not only through the *pars tendinea*
(RECKLINGHAUSEN), but also through its *pars musculosa* (BRANDBERG, *Nord. med.
Ark.*, 1871, III.).

THEORY OF PYÆMIA.

After this mostly clinical representation of pyæmia we will give a general
pathological representation, as far as such is possible by the comparison of
observations on man with the very numerous experimental investigations.
The latter bear partly on the origin of pyæmia in general and of its two

forms, partly on the relation of one to the other, partly on the nature of the active substance. The latest examinations in regard to vegetable parasites have made it very probable, not only that these are the active agents, but also—what has been clinically quite generally accepted—that septicæmia and pyæmia owe their origin to different plants (the first to rod-bacteria, the latter to globular bacteria), and finally that both may combine. Before giving the general pathological observations on both forms of pyæmia, some points must yet be mentioned, which belong equally to both affections.

Pyæmia (septico-pyæmia) originates from a noxious substance which develops in the primary lesion spontaneously, or which is brought there from without.

In favor of the spontaneous origin of this substance are those cases which occur after extensive contusions with diffused extravasations of blood, or after other severe injuries; or, finally, without preceding trauma, even if the skin is unbroken, if the injured are in healthy localities; if, lastly, all other sources of infection are in all probability excluded, symptoms of septicæmia or of embolic pyæmia occur. Many cases of so-called primary acute ulcerating endocarditis also speak in favor of this genesis.

Much more frequently, however, the noxious substance comes from without into the primary lesion or wound. The substance is then either a fluid, which is brought from the wound of a similarly sick person by the finger, instruments, bandages, etc., of a physician or nurse: as in operations of every kind, in women during and after parturition, in the so-called *post mortem* wound; or the access of air contaminated by chemical or parasitical noxious substances is sufficient to produce changes in the wound, which induce pyæmia. Both forms of infection probably occur through the frequent epidemic and especially endemic appearance of pyæmia and puerperal fever, as well in hospitals and lying-in wards, as in private practice. The latter particularly has given unquestionable evidence, which can hardly be explained but by the infection theory, for puerperal fever.

These and many other experiences, particularly that neither the extent and severity of the injury nor the kind of injured tissues are the only cause of pyæmia, undoubtedly prove that the disease in the vast majority of cases does not arise spontaneously, but that it is of miasmatic or contagious origin. Lately most authorities have stated their belief in its contagious or contagious-miasmatic origin; *i.e.*, that the disease arises usually from a similarly diseased individual: but it can also be brought from suppurating or ichorous surfaces of non-pyæmics, especially where many such patients lie in the same poorly ventilated rooms, or where pus, ichor, etc., of such patients (after death) decompose.

Just as widely spread, and partly better founded, is the opinion in regard to the contagious nature of puerperal fever. The contagium is brought by physicians, students, midwives and nurses, sometimes directly, sometimes by instruments, bandages, or cloths, upon wounded skin or mucous membrane of the genitals, whence it gets directly into the blood, or where it first occasions infection of residues of blood, placenta and decidua, which are present within the genitals, of the lochiæ, etc., and secondarily one of the above mentioned affections, most frequently endometritis and diffused metritis.

Private practice gives more remarkable and demonstrable examples for this, than hospital practice. In regard to the former, a number of careful observers (WEG-SCHEIDER, WINCKEL, VEIT, WERDTMÜLLER, STEHBERG, MAYER, KAUFMANN, AHLFELD, and others) have stated, that puerperal fever is restricted exclusively or almost so, to the practice of a few accoucheurs or midwives, or that it is transported

from place to place from lying-in-wards, or from a private residence by physicians, midwives or nurses, who have come in contact with those who had been sick with or died from puerperal fever, with portions of their bodies or with the clothes or bed-linen infected by them.

The sporadic cases undoubtedly originate most frequently by infection with the puerperal septic substance. But they may arise, just as the first case of an epidemic or eudemic, by infection of some other material, not originating in sick parturient women : through pregnant women, suffering from phlegmons of different kinds, from ulcers, *e.g.*, of the extremities, through physicians and students, who bring with their fingers, clothes, or instruments septic substances from those sick with other diseases or from their bodies.

But observations in lying-in wards also speak much more in favor of the contagious nature of puerperal fever. Women who are received in lying-in wards after their confinement have great immunity from the child-bed fever ; even those received during labor rarely become affected. Most frequently those become sick who come into the institution a short time (one to a few days) before their confinement. In favor of its contagiousness are furthermore the fluctuations, which occur in the time of the appearance of puerperal fever, especially if we accept a stage of incubation of 24–48 hours' duration. The first symptoms appear usually only on the second or third day after the confinement, thus 1–2 days after the period in which examinations were made most frequently, and in which the not rarely injured genitals can be easily touched and infected by the examiner. The appearance of puerperal fever in the newly born infant also makes the above opinion probable. If they die during or immediately after birth, the infection has been affected by the blood of the mother infected already previously to or during parturition. If the child sicken later, it has become infected most frequently at the umbilical wound by the mother or the nurses directly, or by means of the clothes.

Against the miasmatic nature of pyæmia as well as of puerperal fever, is the fact that their occurrence and their propagation is not dependent upon any peculiar constitution of the air ; that they occur in all degrees of latitude, by the same conditions of the weather, etc. ; that the seasons of the year (winter) only influence them indirectly ; the greater prevalence of puerperal fever in lying-in wards, the differences which the diverse institutions show, the fluctuations in the proportion of mortality, which occur in the same house at different times, speak at least as much in favor of its contagious as of its miasmatic nature. (See the numerous statistics of child-bed fever by VEIT.)

The substance brought into, or originating spontaneously in the primary wound changes it so much, that the alteration is visible. (*Vide* p. 591.)

The microscopic changes of such wounds have been examined more particularly within the last years: partly in regard to the composition of the pus, especially its inclusion of bacteria, partly in regard to the action of the bloodvessels, through which absorption of the noxious substance occurs. At newly made wounds this absorption can take place directly, as from the moment of reception of the injury first unaltered, later putrid substances (extravasated blood, tissue-fluids, even portions of the tissues) are received through the torn vascular and lymphatic vessels, until a closure of the same occurs by compression or thrombosis (*vide infra*).

In well-granulating and suppurating wounds no communication seems to take place, under normal circumstances, between the surface of the wound and the vessels lying at its base. Most medicaments brought upon such wounds do not penetrate into the general circulation, unless they act as caustics. Putrid substances put upon the surfaces of wounds in animals have no general consequences, while such do arise if much smaller quantities of the same substance are injected into the subcutaneous cellular tissue or into the veins. In normally granulating suppurating wounds the arteries are probably rapidly closed by organizing thrombi. The veins are usually quite collapsed and much folded; only if they were already previously diseased, as well as in abnormal general conditions, thrombi are formed within them. If these organize, then absorption of noxious sub-

stances is only possible in the beginning. But if they soften, if at the same time a loosening of their coats takes place through serous or purulent infiltration, noxious substances can enter the more readily the nearer they are to the wall of the veins; they saturate the thrombus and penetrate with it, as soon as it becomes an embolus, into the affected organs. The capillary vessels of the surface of the wound are compressed at first by the œdema, later by the granulation-tissue, but are likely to reopen, until their lumen has definitively disappeared. But such an absorption may take place by the newly-formed capillaries. The transmigration of cells into the bloodvessels, proven within the last years, which has been seen in the colorless blood-corpuscles, in pigment-cells and in the common (immovable) connective-tissue corpuscles, is very important in regard to the absorption of noxious substances into the vascular system: for as well as lymph-corpuscles with coloring matter, so may they, containing bacteria, penetrate through the vessel's wall into its lumen, alter the thrombus, etc. (*vide infra*).

Some ascribe the greatest importance to the lymphatic vessels in the absorption of septic substances. What part they take in the regular healing of wounds and in suppuration, we do not know; the lymphatic glands remain normal. In ichorous suppurations, on the contrary, demonstrable lymphangioïtis and lymphadenitis are present already even during life. BILLROTH has demonstrated by injections, that the lymphatic vessels become closed at the wound, that they do not end there as open tubes, that the granulations have no lymphatic vessels, that these are only formed anew in the cicatrix with the transformation of the gelatine-like intercellular substance of the granulations into connective tissue.

The lymphatic glands may perhaps retain the noxious substance to a certain degree. But as it is here in intimate connection with their numerous capillaries, another source for the absorption of such substances exists in the presence of the bloodvessels.

The absorption of the septic substance probably only takes place at the point of the injury situated externally or within the body. This is proven partly by innumerable experiences in practice (only slight danger in all injuries, especially of the bones, if the skin be unbroken); partly by experimental observations (difficulty of resorption of septic poison by uninjured respiratory or digestive mucous membrane).

Within what period of time absorption of septic substances occurs at the wound, we do not know. In some cases it probably continues as long as such substances are present, and as long as their resorption is possible by the vascular or lymphatic vessels. At other times only one shorter or longer period of absorption takes place: it causes traumatic fever, or a short attack of fever later arising. In still other cases absorption occurs repeatedly, daily once or several times: many believe the chills of pyæmia to be a symptom of such absorption.

Microscopic demonstrations of the absorption of noxious substances into the blood, lungs, etc., have been already given, at least for fat. But only lately has it been shown by clinical observation and experiment, that diverse substances are causes of pyæmia, and different substances have been demonstrated to be the generators of septicæmia and of pyæmia proper.

That fluid substances are absorbed from the wound has been frequently proven for liquid fat. I found it as well in newly inflicted injuries as in suppurations especially of the bones, and advanced the hypothesis that other not microscopically demonstrable substances can get with it from the pus-centre into the blood, etc. (l.c.). BUSCH (*Virch. Arch.*, XXXV., p. 325) demonstrated, that fat is absorbed as well by blood as by lymphatic vessels: he injected carmine mixed with oil into the destroyed medullary canal, and found carmine particles as well in the larger veins of the extre-

mities as also in the lymphatic glands. More rarely an albuminous embolus of the lung capillaries was found (COHN, *Klin. d. embol. Gefässkrkh.*, p. 338.—The AUTHOR, l. c.)

The numerous experimental investigations for the discovery of the nature and the consequences of the noxious substances have not yet led to a generally received opinion. For neither the nature of the substance in general, nor of that causing either septicæmia or true pyæmia separately, nor the relation of one to the other, is as yet definitively known. It is most probable that both forms of pyæmia are distinct, that they usually occur separately, but are occasionally also combined.

In the experimental researches upon SEPTICÆMIA, animals, most frequently dogs (rabbits and guinea-pigs react too strongly to the substances used, to be advantageously employed); more rarely cats, horses, sheep, were injected with putrid substances of different kinds, as blood, albumen, muscular substance, lime, secretion from a wound, also putrid vegetable substances. The substances were usually carefully filtered, to avoid disturbing actions of a coarsely embolic nature. They were injected into the stomach and large intestine, also into the crop of birds, into the subcutaneous cellular tissue or into the pleural cavity, most frequently into the veins : in the former the phenomena appeared more slowly and were milder, were even entirely absent; in the last they appeared more rapidly and were more intense. Sometimes, large quantities were injected at once; sometimes, in order to imitate the natural processes as nearly as possible, small amounts were inserted repeatedly. But the latter modification has the disadvantage, that in its consequence numerous external wounds, and therefrom the possibility of thromboses, arise. At the point of the injection almost always intense inflammatory appearances set in.

Such experiments were first made by GASPARD, later by MAGENDIE, STICH, VIRCHOW, PANUM, BILLROTH, O. WEBER, SCHWENINGER, HEMMER, BERGMANN, HUETER, KLEBS, and others.
The action of putrid liquids is not dependent upon the individuality of the animal. The quantity of the solution necessary to produce death is in exact proportion to the size and weight of the animals. The duration of decay and extraneous circumstances influence the intensity of the action : by a temperature of 30–40° C. diverse solutions produced their maximum action in five to eight days. (BERGMANN, also previously VIRCHOW and STICH.)

The symptoms of this experimental putrid poisoning were in many respects similar to those of septicæmia. Smaller well-filtered amounts, repeatedly injected, instantly occasioned restlessness in the animal; very soon efforts to vomit and vomiting, already after a few hours usually intense fever with temperatures to 40° C. and more, mostly with a very weak and rapid pulse and greatly hastened respiration. At the same time usually intense nervous disorders, at times more of a spinal, at others more of cerebral nature, again more dependent upon the sympathetic, appeared; moreover, great debility, muscular trembling, *subsultus tendinum*, vomiting. The almost constant diarrhœa was at first feculent, then catarrhal, at last often dysenteric, usually very profuse. The sclerotic was icteric. In pure cases metastatic inflammations of the lungs, etc., as also of the serous membranes, were absent.

The intensity of the symptoms was in direct proportion to the amount of the injected fluid. Small amounts only produced moderate fever, or also vomiting, etc. Larger amounts had the consequences described above.

Still larger quantities, injected at once or in quick repetition, caused rapid death.

Death is followed by an extraordinarily rapid decay. The blood of the fresh body (as well as that taken from the artery of the living person) is dark-brown, tar-like, does not oxidize, coagulates badly, its corpuscles are partly dissolved, and its serum colored red. The other stated blood-changes (acid reaction: formation of carbonate and hydrothionate of ammonia, or of lactic acid, diminished amount of fibrin, destruction of the blood-corpuscles) are probably phenomena of putrefaction. The great imbibition by the vessels' coats of the coloring matter of the blood is probably due to the same cause. Whether a decrease of the blood-corpuscles occurs in consequence of diminished reproduction, is questionable. The mucous membrane of the stomach, and especially of the intestine, constantly shows intense, frequently hæmorrhagic inflammations, now of a common catarrhal nature, now of so-called croupous or even diphtheritic character, frequently with great enlargement of the intestinal follicles. The mesenteric vessels are abundantly filled. The lungs, kidneys, brain, and liver are also usually hyperæmic or contain numerous hæmorrhages. Relatively rarely inflammations, frequently slight hæmorrhages, occur in the serous membranes and in the joints.

Fresh blood of a venesection in a healthy man can neither induce fermentation of sugar nor of urea, amygdalin and asparagin; that of individuals who, on the contrary, suffer with infectious diseases, even in a few hours causes not only sugar and urea, but also amygdalin to ferment (SCHMIDT).

Metastatic deposits were usually not found in these cases, if the injected masses were well filtered and the experiment itself was conducted with the necessary care. But occasionally metastases did occur. They were caused probably always by the bloody injury to the skin or vein necessary to making the experiment, particularly by fresh or by later-forming blood-coagula on the veins' walls; perhaps also by the occurrence, in the animals who lived for a longer time after the experiment, of debility of the heart and muscles (marantic thrombosis). It is undecided whether putrid infection increases directly the tendency to coagulation of blood within the vessels. The secondary purulent or ichorous foci henceforth do not only act infectingly upon their surrounding parts, but also upon distant parts: partly because from them new emboli, saturated with ichor, get into the circulation, partly by fluid substances of the same kind.

The experiments by PANUM and O. WEBER of injecting putrid fluids (without solid elements), sulphuretted hydrogen, sulphuret of ammonium, butyric acid and ammonia, did not cause coagulation within the capillary vessels.

To determine the nature of the septic or putrid substances, different means have been tried. The undoubtedly existing and chemically demonstrable substances in septic poison were injected into animals, and the consequently occurring symptoms compared to those of a putrid substance. By different observers sometimes the products of decomposition of the albuminates (leucin, butyric acid, valerianic acid), sometimes those of protagon (glycerin-phosphoric acid, solid fatty acids), but most frequently sulphuretted hydrogen, sulphuret of ammonium, and carbonate of ammonia, have been thought essential.

A concurrence of all experimenters, from GASPARD and MAGENDIE to BILLROTH and WEBER, is still wanting: no one of those materials is just like the putrid substance.

According to others the septic poison is an albuminous substance in the act of metamorphosis. Its action can be supposed to be one of fermentation : it induces a process of fermentation within the blood.

The older experiments in regard to this were made by THIERSCH, the later ones by HEMMER and SCHWENINGER.

Lastly, in order to determine the nature of the septic substance, it has been attempted to isolate its active portions. The almost pure substance, SULPHATE OF SEPSIN, thus produced, has the same action as common putrid poison.

According to PANUM, the real putrid poison is not identical with any one of the chemical combinations or any one of the substances, which have until now been isolated by chemical analysis of the products of decomposition of nitrogenous substances. It is probably a concealed ferment belonging to the so-called extractive matters (carbonate of ammonia, leucin, tyrosin, fatty acid, acetic acid, etc). It is not volatile, but fixed, is not decomposed by boiling, and is soluble in water. The albuminous substances contained in putrid fluids are not poisonous *per se*, but they condense the poison upon their surface. Putrid poison can only be compared in respect to its intensity to the poison of snakes, curare, and vegetable alkaloids. BERGMANN comes to similar conclusions. According to him, the poisonous action cannot be dependent upon animal or vegetable organisms (MEYERHOFER'S vibrionic theory), as solutions, which were exposed for hours to a temperature of 100° C., maintained their activity. Not the solid ingredients, but the fluids of the products of putrefaction, are the vehicles of the poison. The poison is not volatile, but diffusible. It is not a protein-compound. BERGMANN and SCHMIEDEBERG (*Med. Ctrlbl.*, 1868, No. 32) have produced the sulphate of sepsin in a crystallized condition. It acts upon dogs and frogs exactly like the original putrid substance. BERGMANN (*D. Ztschr. f. Chir.*, 1872, I., p. 373) produced in his latest experiments active and inactive crystals of sulphate of sepsin from putrescent yeast. The former act in the main similar to the mode of putrid fluids, but they are more evanescent in their action, and the intestinal affection is more moderate. B. identifies his sepsin with the putrid poison generated by bacteria in putrefying substances.

ZÜLZER and SONNENSCHEIN (*Berl. klin. Wochr.*, 1869, No. 12) produced from maceration-fluids of the Berlin anatomical institute, a substance which acts like an alkaloid nearly allied to atropia and hyoscyamia.

FISCHER (*Med. Ctrlbl.*, 1869, No. 27) has not yet detected sepsin in putrefying pus. He supposes putrid pus-poisons to be of a peptone-like nature.

The terms septic and putrid are frequently used synonymously. Their distinction is shown especially by the following experiments by DAVAINE (*Bull. de l'acad. de méd.*, 1872, No. 31–38). D. determined how large a quantity of putrid, *i.e.*, simply putrefying blood, and how large a quantity of septicæmic blood, *i.e.*, blood of animals infected with sepsis, was necessary to produce death in animals of a certain species. The blood was injected subcutaneously into the animals (rabbits and guinea-pigs). Of 72 guinea-pigs 25 were killed by 1–10 drops of putrid beef-blood, of 11 others none died which received less than $\frac{1}{10}$ of a drop. Of 48 rabbits 26 were killed by 1–16 drops ; in 9 others the minimum fatal quantity was $\frac{2}{100}$ of a drop. To solve the second question 5 rabbits received 2–15 drops of stinking blood from an ox killed 10 days previously (in July), and died after $1\frac{1}{2}$—26 days. Blood taken from their hearts was injected into a second lot of animals, from these again into a third, and so on to the twenty-fifth generation. The conclusions were : that blood of animals thus septically infected was absolutely more pernicious than simply putrid blood, for it killed without exception in doses in which the latter did not even endanger life, and that it increased in activity by successive infection of consecutive generations, so that finally quite incredibly small amounts of blood produced death ; in the twenty-fourth and twenty-fifth generation it was only one-billionth or one-trillionth part of a drop. In regard also to the rapidity of their action putrid and septic blood differ : the latter kills in less than 40 hours, the former only after days. With neither kind of blood was the occurrence of death in regular proportion to the dose employed (contrarily to blood from gangrenous spleen). But similarly to the blood of gangrenous spleen septic blood diminished in activity by putrefaction.

DAVAINE's experiments upon septicæmia have been partly corroborated, partly not (*Bull. de l'acad. de méd.*, 1873, No. 3–5).

The septic substance is not absorbed by healthy granulating wounds, just as it is not by the normal skin or mucous membranes. Probably also not by the lungs. In favor of this are partly experiments, partly clinical observation, partly also the non-volatile character of the substance. What provisions prevents putrid infection of creatures by their own intestinal contents, we do not know.

In old cutaneous ulcers, in intestinal ulcers, in bronchial ectasias with intact or ulcerated mucous membrane, we very rarely see pyæmic phenomena; frequently even not when upon these common decomposition of the wound's secretion takes place. But the cases of putrid bronchitis recognized in later years partly belong to this class.

DAVAINE (l. c.) has answered the question, whether septic poison also, like the poison of gangrene of the spleen, is transferable by the sting of an insect, affirmatively. He placed a fly under a glass globe together with some blood from a rabbit which had died from septicæmia. After half an hour he abscised the fly's sting and pushed it through a narrow opening under the skin of a strong rabbit. The animal died thirty-five hours later.

LISTER's treatment of wounds prevents, according to L., the occurrence of putrid decomposition in the affected parts, by excluding extraneous agencies which induce an abnormal condition of the wound. (S. SCHULTZE, *Volkmann's klin. Vortr.*, 1873, No. 52.)

Experimental researches relating to PYÆMIA PROPER agree much less than those in regard to septicæmia. They undoubtedly prove that not merely absorption of pus alone produces pyæmia, that even larger quantities of pus, directly injected into the veins, are quite inactive, and that a specific pus probably induces pyæmia (pyogenic in contra-distinction to saprogenic or putrid infection). The main agency is, according to the later examinations, bacteria,—globular bacteria. These either act directly in an injurious manner, or they generate the noxious substance. Whence they originate, whether always only from similarly sick persons, etc., is unknown.

The first hypothesis, to which pyæmia also owes its name, that pus is absorbed in substance at the primary wound and carried away with the blood to a point where the capillaries are too narrow to allow it to pass (*i.e.*, the existence of a real purulent metastasis), could never be proven in any of its propositions: particularly because until lately no morphological distinctions were known between colorless blood- and pus-corpuscles, because the latter are in many parts of the body migrated colorless blood-corpuscles, and finally because pus originates demonstrably at the point of so-called secondary deposit. Less important is the reason that the means by which pus in substance penetrates into the vascular system are unknown to us. First, undoubtedly intravasations or perforations of purulent collections through the vessel-walls into their lumen occur, as long as this is not obstructed by thrombi or by other means. Moreover, we occasionally see a hypopyon, an accumulation of pus in the anterior chamber of the eye, as also other quite undoubted pus-accumulations becoming resorbed. Finally, it has been experimentally demonstrated that pus-corpuscles can penetrate from the surrounding parts of the veins through their wall into their lumen. RECKLINGHAUSEN exposed a vein, ligated one inch of it, first at the cardiac then at the peripheral extremity, dusted carmine into the wound and sewed the skin over it. Suppuration occurred around the vein; the newly-formed pus-corpuscles absorbed the carmine. The thrombus formed in the ligated portion of the vein contained many pus-corpuscles with carmine.

On account of the difficulty of explaining the resorption of pus, PIORRY propounded the opinion that pus originates within the vascular system even in consequence of an inflammation of the blood (hæmitis).

That injection of common pus is occasionally without any effect or only acts tem-

porarily, that with proper precaution no metastases follow, was already demonstrated by the first experiments of D'ARCET, DUPUYTREN, BOYER, GÜNTHER, SÉDILLOT, by the later ones of VIRCHOW, O. WEBER, BILLROTH, and by the latest of HIRSCH-FELD. Only the property of even fresh pus to cause fever (pyrogenic) seems always to exist, according to BILLROTH and WEBER, but HIRSCHFELD found even this not to be constant.

That BACTERIA are the most important agents of pyæmia was only definitively as-certained in the last two years. (See pp. 105 and 106.) Excepting a former remark of VIRCHOW and RINDFLEISCH, RECKLINGHAUSEN, HUETER, and KLEBS were especi-ally the ones who maintained this.

KLEBS (Corr.-Bl. f. schweiz. Aerzte, 1871, I., No. 9; Beitr. z. path. Anat. d. Schusswunden, 1872) gave a more particular description of these conditions, but un-fortunately without separating septicæmia from pyæmia. According to K., infectious diseases of wounds are produced by the microsporon septicum, which occurs as well in those forms accompanied by suppuration, so-called pyæmia, as in the purely septic forms. These fungous growths locally destroy the tissues, cause suppuration, and penetrate into the lymph- and bloodvessels; they are the cause of secondary foci or diffused inflammation. KL. discovered the microsporon as well in the fluids of the wound (healthy and thin pus) as upon the surfaces of tissues (granulations of different kinds, joints, serous membranes). The penetration into the bloodvessels takes place so that the tissues of the vessel-wall are destroyed from without inward: within the vessel coagulation occurs, during the progressive destruction hæmorrhages (so called septic warning or tertiary bleeding) arise. The penetration of the microsporon into the interstices of connective tissue takes place either directly or indirectly, while the germs of migrating cells are absorbed. Hereby the permanent connective-tissue cells are destroyed, the white blood-corpuscles migrate. Secondary interstitial myositis originates similarly. The secondary changes in the organs, especially purulent cen-tres of the lungs, are also due to the fungi. Most remarkable are the fungus-metas-tases, according to KLEBS' description, in the liver, etc. In a case of multiple osteo-myelitis, KL. also detected fungi. In the development of the microsporon sep-ticum there originates a substance producing fever, diffusing itself through the nutri-tive fluid; continued fever is only caused by continued introduction of this sub-stance, with presence of the fungi within the organism.

At KLEBS' suggestion, ZAHN (Z. Lehre v. d. Entz. und Eiterung. Bern., Diss., 1871) discovered that the microsporon septicum induces inflammation and suppuration, and TIEGEL (Ueb. d. fiebererreg. Eigensch. des Microsp. Sept., Bern. Diss., 1871) that it possesses properties which induce fever, and that the fever produced by it is identical with that generated by sepsin.

Contrary to KLEBS (see p. 105), WOLFF (Med. Ctrlbl., 1873, Nos. 8 u. 9) observed only graded differences between a filtered solution and the residue containing fungi. In numerous subcutaneous injections into guinea-pigs he found that putrid blood in its own form acts differently than when filtered, even with the addition of bacteria; that therefore the deleterious effect of the former must be due not to the bacteria, but to some other morphological or chemical ingredient of the residue. W. did not succeed in producing in rabbits and guinea-pigs, by introduction of concentrated fluids containing fungi into the air-passages (by tracheotomy or by inhalation), putrid changes of the lungs' parenchyma, diphtheria, or miliary abscesses composed of colonies of bacteria. Only pneumonias arose, similar to those which occur at other times in such animals, without any demonstrable invasion of bacteria. WOLFF (Ib., 1873, No. 32), who separates embolic from septic pyæmia, discovered that the fluid con-taining pyæmic and septic fungi is much less deleterious than pyæmic and septic secretion of wounds, which, injected in the same dose, is almost absolutely fatal. W. cannot, from the results of his examinations, ascribe the deleterious action, at least not exclusively, to the bacteria in the wound's secretions. Neither does he acknowledge globular bacteria to be the special cause of pyæmia, or rod-bacteria that of septicæmia.

HUETER had previously (Berl. klin. Wschr., 1869, No. 33) maintained that septic erysipelas was generated and propagated by the migrations of monads or micro-cocci in the skin. Later (Ib., 1870, No. 8) H. described diphtheritic myositis, which is produced in rabbits by the introduction of croupous membranes, even if these have been dried and pulverized. In a later work (Volkmann's Samml. klin. Vortr., 1871, No. 22) H. states that diphtheria and erysipelas of wounds are produced by the migration of monads into the living tissues. Furthermore, he originated the term diphtheritic phlegmon: i. e., a rapidly progressing inflammation, which is propagated by the migration of the monads, which quickly leads to hyperæmia and swelling of

the tissues, and which rapidly culminates in formation of a stinking pus. By this and a later work (*D. Ztschr. f. Chir.*, 1872, I., p. 91) H. believes to have demonstrated that the process of putrefaction of the blood has something peculiar, consisting in the fact that the aërobiæ (*i.e.*, monads, whose existence is dependent upon the presence of oxygen) develop therein in large numbers and exist for a long period. These monads penetrate in large quantities into the living tissues and into the circulation ; they can go thence into the secretions of the body, and in consequence of their appearance in large numbers, inflammatory processes of a certain character arise. But generators of putrefaction can also penetrate through the vessels' walls into venous thrombi ; which, changed into emboli, get into the lungs and cause there also a diphtheritic inflammation. Several days after the injury pus is produced, whose putrefaction has the same morphological course as that of the blood ; here also the aërobiæ are the predominating generators of putrefaction.

VOGT (*Med. Ctrlbl.*, 1872, No. 44) detected in a living pyæmic soon after a metastatic pus-centre appeared in the wrist, in it, migrations of immense quantities of monads with vigorous vital movements, while these appeared only singly in the corresponding healthy joint, as also in the blood generally. (V. did not see any rod-bacteria.) This condition continued during five days until death, and could be seen for twenty-four hours *post mortem* in the same way.

HUETER first explained erysipelas of wounds as produced by migration of monads. NEPVEU (*Gaz. méd. de Par.*, 1872, No. 3) detected bacteria in traumatic and spontaneous erysipelas. According to ORTH (*Arch. f. exp. Path.*, 1873, I., p. 81), the bacteria of erysipelas are the same as COHN'S globular bacteria. In inoculated animals he also found some of long forms, but these never showed any motion.

Examinations in regard to the influence of bacteria upon the origin of puerperal fever have resulted similarly. The first observations were made by COZE and FELTZ (*Gaz. méd. de Strasb.*, 1869, Nos. 1–4). WALDEYER (*Arch. f. Gynäk.*, 1872, III., p. 293) detected bacteria in the diphtheritic form of puerperal fever, in the diphtheritic deposits upon the interior surface of the uterus, in the puriform masses from the lymphatic vessels of the uterus and *ligamenta lata*, in the peritoneal exudation, etc. Everywhere they were contained within the pus-corpuscles. The bacteria were globular bacteria, more of an oval shape, 2, 4, 8–10 connected in short chains ; another time W. saw also rod-bacteria. According to WALDEYER also, the dark masses in *parametritis diphtheritica* (VIRCHOW), as well as the yellow substances, believed to be puriform broken-down thrombi in the lymphatic vessels of the uterus, are for the greater part composed of bacteria.

The investigations by HIRSCHFELD (*Arch. d. Heilk.*, 1873, XIV., p. 193) are the more important, as they prove a parallelism between the number of bacteria and the clinical picture, and show the marked distinction between pyæmia and septicæmia. According to H., the pus-corpuscles of healthy fresh pus are equally large, round, with sharp outline, whitish and shining, without visible nucleus ; the serum is perfectly clear, any solid masses in it are soluble in ether or potassa solution ; at the most there are some few putrefaction-bacteria (*bacteria termo et lineola*) present. According to BURDON-SANDERSON (l. c.), healthy pus does not occasion cloudiness in Pasteur's fluid (that is no production of bacteria). In pyæmic pus the pus-corpuscles are of greatly varying volume, with less distinct and regular outlines, frequently as though prickly and scolloped ; their protoplasm is darker, grayish-black, roughly granular, the nuclei are frequently apparent without preparation ; the cells show usually extensive formations of vacuoles. The granular appearance is due to globular bacteria, which are deposited upon the cells and penetrate into their protoplasm. These bacteria (see p. 89) are at first small granules, usually collected in pairs and then measuring two to four mm. ; in the next few days they form chains of eight links ; they are immovable ; they do not change in ether, potassa solutions, acetic acid. In severe cases of pyæmia the globular bacteria of the pus-corpuscles as well as those of the *liquor puris* become constantly more numerous ; the latter soon consists almost entirely of them. Then formations of colonies appear ; H. never found any formation of zooglœa. (Also see ORTH. *Arch. d. Heilk.*, 1872, p. 265.) The pus also has a peculiar odor. The wound presents a more or less characteristic appearance ; the degree of the change is *ceteris paribus* proportionate to the number of globular bacteria. In the same way the severity and rapidity of the course of the constitutional affection is in proportion to the number of bacteria which are demonstrated to be within the blood. In persons who have had limbs recently amputated, the appearance of numerous bacteria in the secretion of the wound is usually very soon followed by the presence of the like bacteria in the blood. Toward the fatal termination H. found that occasionally two to three free (usually only consisting of

two links) bacteria to one red blood-corpuscle. In the higher degrees of infection the white blood-corpuscles presented the same appearance as the cells of the infected pus. Those corpuscles are themselves increased. The red blood-corpuscles present no change excepting an incomplete formation of rouleaux.

The relation of septicæmia to pyæmia H. discovered by subcutaneous injectious of very minute amounts of pus, usually only one drop. Injection of healthy pus usually caused no local and constitutional symptoms, or only slight fever. After injection of pus containing various amounts of globular bacteria (usually from pyæmic patients), intense irregularly intermittent fever (more than 42° C.) suddenly set in, on the seventh to the ninth day; the animals emaciated and died almost without exception on the sixteenth to the twenty-fourth day. If the pus was rich in globular bacteria in the form of colonies, the severe symptoms appeared on the third, death on the seventh day. On dissection extensive suppuration of the cellular tissue was found at the point of the injection; within the pus numerous, within the blood usually few (more numerous toward the end) globular bacteria. Most frequently, of the internal organs, the kidneys were diseased (granular degeneration, not rarely with bacteria), also the spleen, rarely the liver and lungs. Injection of putrid pus, *i.e.* containing numerous bacteria of putrefaction (*bact. termo et lineola*), (partly putrid secretions of wounds, partly such as had become putrid by being kept a long time) gave in the main the same results as observed by other experimenters, lately by BERGMANN. H. also communicates several experiments which illustrate partly the pyæmic, partly the putrid action of pus, such as that of injecting a fluid from erysipelas of a wound.

HUETER (*D. Z. f. Chir.*, 1872, I., p. 91) distinguishes pyæmia from septicæmia, but believes the former to originate from monads, the latter from vibrios; and says that he has found a difference in the injection of putrid blood and pus and that of other putrid infusions (muscles). H. classifies diphtheritic inflammation with septic and pyæmic diseases. Most peculiar is the opinion of EBERTH with respect to the latter (*Z. K. d. bacterit. Mykosen*, 1872), according to whom the same bacteria not only cause pyæmia and septicæmia, but also diphtheria.

XVI. Fever.

CURRIE, *Med. Rep. on the Eff. of Water as a Rem. in Febr. Dis.*, 1797.—REIL, *Erkentniss u. Cur der Fieber*, 1799.—CHOSSAT, *Mém. sur l'infl. du syst. nerv. sur la chaleur animale*, 1820; *Rech. expér. sur l'inanition*, 1843.—J. DAVY, *Physiol. and Anatom. Researches*, 1839 and 1863.—GIERSE, *Quænam sit ratio caloris organici*, Hal., 1842.—HEINE, *Physiol.-path. Studien*, 1842.—STANNIUS, Art. "*Fieber*," in *R. Wagner's Handwörterb. d. Physiol.*, 1842, I., p. 471.—WUNDERLICH, *Arch. f. phys. Heilk.*, 1842, I.; 1843, II., 1856, 1857, I.; 1858, II.; *Arch. d. Heilk.*, I., pp. 97 et 385; II., pp. 433 et 547; III., pp. 13 et 97; IV., p. 331; V., pp. 57 et 205; VI., p. 14; VII., pp. 129, 267, 350, 434; VIII., p. 36; IX., p. 1; X., p. 314; *Das Verhalten der Eigenwärme in Krankh.*, 2 Aufl., 1870.—HIRSCH, *Beitr. z. Erkenntn. u. Heil. d. Spinalneurose*, 1843.—HALLMANN, *Zweckmäss. Behandlung des Typhus*, 1844.—ROGER, *Arch. gén.*, 1844, et seq.—BERGMANN, *Müller's Arch.*, 1845, p. 209.—J. R. MAYER, *Die organ. Bewegung in ihrem Zusammenhang mit dem Stoffwechsel*, 1845.—HEIDENHAIN, *Das Fieber an sich und das nervöse Fieber*, 1845.—HELMHOLTZ, *Im Berl. encyclop. Wörterb. d. med. Wissensch.*, 1846, XXV., p. 323.—ZIMMERMANN, *Preuss. med. Vereinszeit*, 1846, Nos. 30 et 40; 1847, No. 19-21, 35-36; 1859, No. 14-16, 22 et 58; *Prag. Vjschr.*, 1847, IV., p. 1; 1852, IV., p. 97; *Arch. f. phys. Heilk.*, 1850, p. 283.—RUETE, *Beitr. zur Phys. des Fiebers*, 1848.—SCHMITZ, *De calore in morbo*, *Diss. Bonn.*, 1849.—TRAUBE, *Charité-Annal.*, 1850, I., p. 622; II., p. 19; *Deutsche Klin.*, 1851, 1852, 1855, 1862; *Med. Ctrdz.*, 1863, No. 52, 54, et 102.—V. BARENSPRUNG, *Müll. Arch.*, 1851 et 1852.—HEISE, *De herb. Digit. in morb. febril. chron. adhib. vi antiphlogistica*, *Berl. Diss.*, 1852.—LICHTENFELS et FRÖHLICH, *Denkschr. d. Wien. Acad.*, 1852, III., 2. Abth., p. 113.—DAMROSCH, *Deutsche Klin.*, 1853, p. 313.—FICK, *Müll.'s Arch.*, 1853; *Med. Physik.*, 1856.—JOCHMANN, *Beob. über die Körperwärme in chron. Krankh.*, 1853.—G. V. LIEBIG, *Ueb. die Temperaturuntersch. des ven. u. arter. Blutes*, 1853.—NASSE, Art. "*Thierische Wärme*," in *R. Wagner's Handw. d. Phys.*, 1853, IV., p. 1.—HECKER, *Charité-Annal.*, 1854, V., p. 343.—VIRCHOW, *Handb. d. Spec. Pathol.*, 1854, I., p. 26.—PARKES, *Med. T. and G.*, 1855, No. 246 ff.—L. WACHSMUTH, *De ureæ in morbis febril. auct. excret.*, 1855.—THIERFELDER, *Arch. f. phys. Heilk.*, 1855.—THIERFELDER et UHLE, *Ibid.*, 1856.—

SEUME, *De calore corp. humani in morte observ.*, Lips., 1856.— MAREY, *Compt.-rend.*, 1856, Mars et Avril; 1858, Nov.; *Gaz. méd. de Paris*, 1857 et 1859; *Rech. sur la circulat. du sang à l'état phys. et dans les mal.*, 1859; *Journ. de phys.*, 1859; *Rech. sur le pouls au moyen d'un nouv. appareil, le sphygmographe.* 1860; *Arch. gén.*, 1861, Fevr.—MEYER, *Char.-Ann.*, 1858, 2. H.—W. MÜLLER, *Mitth. d. Erlanger med. Soc.*, 1858, 1. II., p. 83.—S. RINGER, *Transact. of the Med.-Chir. Soc.*, 1859, XLII., p. 361; XLV., p. 111.—BERNARD, *Allg. Wien. med. Zeit.*, 1859, No. 23 et seq.—LIEBER-MEISTER, *Deutsche Klin.*, 1859, No. 40; *Arch. f. Anat. u. s. w.*, 1860, p. 520, 1861; *Prag. Vjschr.*, 1865, III., p. 1; *D. Arch. f. klin. med.*, VII., p. 75; VIII., p. 153; X., pp. 89 et 420; *Virch. Arch.*, LII., p. 123; LIII., p. 434; *In Volkmann's S. klin. Vortr.*, 1871, No. 19.—SCHIFF, *Allg. Wien. med. Zeit.*, 1859. No 41.—UHLE, *Arch. f. phys. Heilk.*, 1859; *Wien. med. Wochenschr.*, 1859.—VOGT, *Die fieberunterdrüc-kende Heilmethode*, 1859.—BRAND, *Hydrotherapie des Typhus*, 1861.—GRIESINGER, *Arch. d. Heilk.*, 1861, II., p. 557.—BILLROTH, *Arch. f. klin. Chir.*, 1862 et 1864.—DUCHEK, *Oestr. Jahrb.*, 1862, IV.—WEYRICH, *Die unmerkl. Wasserverdunstung d. menschl. Haut*, 1862.—ZIEMSSEN, *Pleur. u. Pneum. im Kindesalter*, 1862; *Greifsw. Beitr.*, 1863.—A. WACHSMUTH, *Arch. d. Heilk.*, 1863, IV., p. 55; VI., p. 193.—WEIKART, *Arch. d. Heilk.*, 1863, IV., p. 193.—WOLFF, *Arch. d. Heilk.*, 1863, IV., p. 371.—BEHSE, *Beiträge zur Lehre vom Fieber, Diss. Dorpat*, 1864.—KERNIG, *Exper-imentelle Beiträge u. s. w., Diss. Dorpat*, 1864.—THOMAS, *Arch. d. Heilk.*, V., pp. 30, 167, 431, et 527; VI., pp. 118 et 329; VII., pp. 225 et 289; VIII., pp. 49 et 385; IX., p. 17.—VOGEL, *Arch. f. wiss. Heilk.* 1864, No. 6.—WALTHER, *Arch. f. Anat. Phys. u. s. w.*, 1865.—HUPPERT, *Arch. d. Heilk.*, 1866, VII., p. 1; VIII., p. 343; X., pp. 329 et 503.—FRESE, *Exper. Beitr. z. Aetiol. des Fiebers*, 1866.—TSCHESCHI-CHIN, *D. Arch. f. klin. Med.*, 1867, II., p. 588.—JÜRGENSEN, *D. Arch. f. klin. Med.*, 1867, III., p. 166; 1868, IV., p. 323.—UNRUH, *Virch. Arch.*, 1869, XLVIII., p. 227.—NAUNYN, *Berl. klin. Wschr.*, 1869, No. 4.—NAUNYN u. QUINCKE, *Arch. f. Anat., Phys. u. s. w.*, 1869, p. 174.—SENATOR, *Virch. Arch.*, 1869, XLV., p. 351; L., p. 354; LIII., p. 111; *Arch. f. Anat. u. s. w.*, 1872, p. 1; *Ueb. d. fbrh. Proc.*, 1873.—LEYDEN, *D. Arch. f. klin. Med.* 1869, V., p. 273; 1870, VII., p. 536.—HEIDENHAIN, *Arch. f. d. ges. Phys.*, 1870, III., p. 504.—RÖHRIG u. ZUNTZ, *Arch. f. d. ges. Phys.*, 1870, IV., p. 57.—WINTERNITZ, *Virch. Arch.*, LVI., p. 181; *Oest. med. Jahrb.*, 1871, p. 180.—MANASSEÏN, *Virch. Arch.*, LV., p. 413; LVI., p. 220.—E. SEGUIN, *Medical Thermometry and Human Temperature*, New York, 1876.
    See also text-books on Physiology and Pathology.

FEVER is that general condition in which the heat of the body is increased by the action of some internal cause. Remarkable symptoms besides the increased temperature and partly dependent upon it are certain nervous phenomena, also changes in the organs of circulation, respiration and digestion, as well as in the secretions.

A. SYMPTOMS OF FEVER.

INCREASED TEMPERATURE OF THE BODY IS A NECESSARY SYMPTOM OF FEVER; where it is absent, fever does not exist. All other symptoms: chills, nausea, thirst, dryness of the skin, frequent beating of the heart, certain changes in the secretions, etc., may be present: if the objectively demonstrable heat is wanting, we do not include these conditions among the febrile ones.

Nervous symptoms, as headache, aching pains in the back and spine, disinclination to exertion, etc., occur frequently enough, without our being allowed to call them febrile, and then they are usually not accompanied by increased frequency of the pulse. Chills occur frequently without fever. Every severe and sudden cooling of the surface of the body produces the symptoms of a chill, which cannot be distinguished from a fever-chill by mere observation. The best example of this is presented by those who attempt to drown themselves in a cold season and therefore remain for a while in cold water; they shiver with cold, even in bed, long after removal from the water. If a thermometer be applied, it shows neither during the chills nor afterward any increase in temperature. Furthermore, hysterical and epileptic peo-

ple often have slight attacks, without loss of consciousness, which, if they are accompanied by movements up and down of the lower jaw, are especially, as cyanosis of the face is always present, deceptively like chills, but not accompanied by increase of temperature. Further observation of their course prove that they are not febrile.

The importance of the state of body-heat in disease was perfectly appreciated even in ancient times. The majority of authors accepted heat as the pathognomonic symptom of fever, whose Greek as well as Latin designations (πῦρ, πυρετός—febris, originally *ferbris*, from *ferreo*) direct to the increased temperature as the most important symptom. But only in modern times, after the invention of the thermometer, did it become possible to state the deviations of temperature by measurement, and to admit of their intelligent observation.

After SANCTORIUS, the inventor of the thermometer (1638), BOERHAAVE made the first measurements of the temperature of the sick. He says : '' Calor febrilis thermoscopio externus, sensu ægri et rubore urinæ internus cognoscitur.'' VAN SWIETEN gives further information in regard to this matter in his commentaries to BOERHAAVE. Another pupil of BOERHAAVE, DE HÄEN in Vienna, continued the measurements of temperature methodically, and first published numbers in his *Ratio medendi*. DE HÄEN discovered already in 1760, that in the chill of fever the temperature of the body is increased by several degrees. In 1797 CURRIE's studies were published, but they did not receive due consideration by his contemporaries. The influence of the nervous system upon the production of animal heat was defended 1811 by BRODIE ; opposed to him was, among others, JOHN DAVY, 1814. In 1821 HUFELAND directed some experiments upon animal heat. Worthy of consideration are the investigations by BRESCHET and BECQUEREL on the heat of the different parts of the body, which appeared in 1835, as also later explorations by DAVY (1839) and these by MAYER (1842). These were followed by more important works : 1841, ANDRÆ ; 1842, GIERSE ; 1843, CHOSSAT ; 1844, HALLMANN and ROGER. In 1846 ZIMMERMANN began his investigations, and he pushed with untiring energy the application of thermometry at the bedside. In 1850 the influential publications of TRAUBE appeared ; in 1851 the classical work by von BÄRENSPRUNG. From these years also date the regular and consequentially prosecuted investigations on the pathological conditions of temperature in the Leipzig Clinic : by WUNDERLICH and his pupils. W. later has the credit of having untiringly pointed out the great practical value of thermometry, and of having thereby induced many to become advocates of this method. Since 1860 the explanation of the conditions of febrile temperatures has been especially sought for by observation and experiment.*

Most frequently in modern times observations of temperature in patients have been made in the axilla and rectum ; now and then the vagina has been used, especially in obstetrical clinics and in cholera, as also the external auditory canal in those mentally diseased. The rectum and vagina have the advantage over the axilla of being always perfectly equally warm, so that in them the thermometer attains its maximum degree after about five minutes. But the skin of the axilla is under ordinary circumstances more or less cooled, and must therefore be thoroughly warmed to the same degree as the internal parts in the neighborhood, before the measurement can be completed. This equal warmth is attained by closure of the axilla, *i.e.*, by air-tight pressure of the upper arm upon the chest, whereby it becomes so to speak an internal part of the body. The time necessary to do this of course varies ; on the average 10–15 minutes. In feverish conditions, especially at the time of the so-called fever-heat, the equable warming of the axilla requires a shorter time than in normal temperature, and especially than in a state of collapse. On account of the necessity of closing and thus warming the axilla equally for the purpose of taking the temperature the time required is considerably longer than if the rectum is

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* It may not be improper to record in this place that in America the thermometer was first used in a systematic way in the New York Hospital, during the winter of 1865-6, by Dr. W. H. Draper and the Editor. Also that, subsequently, the spread of thermometry has been largely due to the writings and personal efforts of Dr. Edward Seguin, of New York.—[ED.]

used. For the same reason it is not possible, by warming the thermometer (to any degree) before placing it into the axilla, to attain an accurate result any sooner than otherwise.

If peculiarity in the course of the disease does not require certain hours, it is best to institute the measurements in the morning between 7–9 o'clock and in the afternoon between 4–6 o'clock ; that is, twice a day. Two observations are sufficient in most cases ; the above-mentioned hours are advisable, because the temperature in febrile diseases is usually lowest at about the first-mentioned time, and highest at the last-mentioned.

The measurement had best be taken by the attending physician himself or by a trustworthy medical assistant ; this ought unquestionably be done, if the results of the observations are to be of scientific application. But if the case be only of practical interest for the physician, an experienced and trustworthy layman may be substituted, as long as the later is controlled and corrected by the physician if the statements appear remarkable or not consistent with the observation of the physician. For certain purposes (the temperature during agony), and if the reading of the thermometer is not to be entrusted to the patient himself, self-registering thermometers are used. In these the uppermost part (measuring 1 cent.) of the mercurial column is separated by an air-buble, and remains stationary when the lower part of the column descends after removal of the instrument.

A knowledge of the condition of the heat of the healthy body is the basis for every judgment of the results of thermometry in the sick. But it is impossible to maintain positively for certain degrees and under certain circumstances, whether they belong in the range of physiology or pathology ; the limits of both upon thermometrical grounds cannot be sharply defined. But it is near the truth, especially by reason of numerous observations upon cured patients or those nearly well toward the end of their convalescence, if we accept as the lowest limit of the normal temperature within the axilla of adults 36.2°–36.3° C. ; as highest limit, 37.5° C. Rectum and vagina are about one-half a degree warmer, their limits therefore 36.8°–38.0° C. All temperatures which pass these limits are at the least suspicious, and dare only be declared normal under particular circumstances and influences. If now the body-heat of man is believed to be the result of continual productions and losses of varying magnitude, it must appear very singular that with doubtless numerous and changeable processes the temperature of the healthy body is almost at a constant height, and that it fluctuates only almost within the limits of a single degree.

Mammalia and birds also possess an almost constant temperature, *i.e.*, their animal heat is more or less independent of the warmth of the medium in which they exist ; while in other (cold-blooded) animals it is considerably influenced by the temperature of the medium : still the constancy of the temperature of man is, though not absolute, particularly great, and the variations occurring in a healthy condition are under all circumstances only moderate.

Not all parts of the same body have at the same time exactly the same temperature, as there are influences bearing upon local temperature in a positive or negative way : the amount of heat carried by the blood, and by direct conduction to the tissues, the heat produced locally, lastly local loss of heat, are not uniform in different parts of the body. Thus it is that particularly the blood of the upper extremities, at least that of the peripheral cutaneous veins, is, in consequence of the large amount of peripheral abstraction of heat, considerably cooler than the blood of better protected parts, *e.g.*, the rectum and vagina, and this may already explain the difference of temperature in these parts and in the closed axilla.

Still more considerable are the differences in temperature between these cavities and the really peripheral parts, *e.g.*, the fingers, toes, ears, nose, etc., whose temperature because of moderate local production is decidedly influenced by the amount of loss of heat. The amount of that difference can only be determined with great accuracy by thermo-electrical means. The internal parts of the body are the warmest, partly because they are best protected from loss of heat, partly because the change of tissues and thereby the generation of heat is more rapid in them than in the periphery, excepting the moderately warm muscles (JACOBSON found only a difference of 0.5 - 1.8° C. between them and the very warm liver: *vide infra*). JACOBSON and BERN-HARDT (*Med. Ctrlbl.*, 1868, p. 643) found by thermo-electrical means almost always the blood of the left heart warmer than that of the right, the difference amounting to 0.12 -0.42° C. HEIDENHAIN and KÖRNER (*Arch. f. d. g. Phys.*, IV., p. 558) maintain, as did also previous observers (G. v. LIEBIG, CL. BERNARD) the contrary ; H. considers as the cause of the higher temperature in the right ventricle, the fact that warmth is brought to its walls from the abdominal cavity. The temperature-measurements in both ventricles do not show figures for the temperature of arterial and mixed venous blood, but values, which are composed of the temperature of the blood and of the walls of the ventricles. This is proven by the fact, that by stopping the absorption of heat, or by its abstraction from that part, the difference of temperature between the ventricles is diminished, is made to cease, or is even reversed ; while increased absorption of heat makes it still greater. This circumstance speaks also particularly for the importance of the direct conduction of heat from layer to layer, in opposition to the equalization of the temperatures of the different parts of the body by means of the circulation. JACOBSON and BERNHARDT found the pleural cavity constantly 0.2°-0.5° C., the liver only at the most 0.06 -0.1° C., colder than the left heart. The blood from the *vena cava inferior* is, probably mainly through the influx of blood from the hepatic veins, warmer than that of the *vena cava superior ;* the difference of temperature between liver and rectum amounts, according to J. (*Virch. Arch.*, LI., p. 275), to 0.5 -1.0° C. in favor of the former. The temperature of the brain, according to MENDEL (*Virch. Arch.*, L., p 12) and (previously to him) FICK, is several tenths of degrees (0.4°-0.7 -1.0° C.) colder than that of the rectum.

Healthy people do not maintain under different conditions the same degree of temperature. If, according to numerous observations, differences appear in different persons of the same age and sex, they are still more considerable in persons of different ages. The unborn child is a very little warmer than the vagina and uterus of the mother; this difference proves that the child possesses its own sources of heat. At birth, infants show in the rectum a temperature of 37.75° C. on the average; of 37 newly born 26 had more than 37.5° C. and only 1 less than 36.75° C. Directly after birth, and particularly after the first bath, children lose on the average 0.7°-0.8° C. ; they show on the average 37.0° C. Of 22 children only 3 retained more than 37.5° C., and 8 fell below 36.75° C. In the next few days the rectal temperature again rises ; it attains on the average to 37.6° C. This height seems to be retained more or less throughout infancy, the daily variations and the influence exerted by extraneous conditions being considerable, while both decrease toward puberty. Toward and during puberty the animal heat is about 0.1° to 0.2° C. less than in early infancy. Healthy adults have the same temperature. Only in the later years of life a minute increase in the average of the temperature occurs, so that senile persons are in this respect like older children.

As regards sex, there is no notable difference of body-heat in individuals of the same age.

Greater deviations of temperature are shown by the same individuals at different times of the day. In general the following may be accepted as constant, although several observations seem to contradict it. The lowest temperature (about 36.5° C. in the axilla) is observed in the healthy in the middle of night, about 1 or 2 o'clock, and remains for a short period or for many hours. After awaking or in early morning generally, *i.e.*, before first

partaking of nourishment, the temperature has frequently already increased by several tenths of degrees, and continues to rise until the hours of forenoon. Then as a rule a slight decrease occurs before midday, but soon after, in the afternoon hours, there is a further rising to the maximum of the day (about 37.5° C. in the axilla), if a considerable temperature has not been already attained during the forenoon. Close to this maximum, which is usually attained in the fifth hour P.M., the temperature remains for a variably long time, so that it afterwards sinks quite slowly; in the later hours of evening this sinking continues usually with greater rapidity until the minimum of the night is reached. The magnitude of this daily fluctuation of the animal heat, its highest and lowest limits, the time of maximum and of minimum, the height and time of occurrence as well as the duration of the occasional forenoon maximum, the rapidity and amount of the daily increase and decrease of the temperature, and the proportionate average temperature are different for unknown reasons in some individuals, even if they are in absolutely the same extraneous circumstances.

These individual differences may partly depend upon different susceptibility to those influences which act in the course of daily life, among which those of work and nourishment are especially to be considered. But certainly the whole daily fluctuation cannot be explained by them: for persons who eat nothing and are inactive during the whole day also present similar fluctuations of temperature. At present it must therefore be accepted as a peculiarity of the organism, not yet understood in its true character. An opinion has meanwhile been given in opposition to the other. According to a preliminary statement by KRIEGER (*Z. für. Biol.*, V., p. 476), the typical course of body-heat is only dependent upon the individual mode of living; it is reversed, "as soon as we sleep by day, wake, eat, drink, and work by night."

All MUSCULAR ACTIVITY increases the temperature. This can already be proven by the muscular force which we expend in order to maintain an erect or sitting posture. Shortly after a reclining position has been taken, the temperature in the axilla begins to fall, and often sinks several tenths of degrees (quite an amount, if we take into account the narrow limit of the daily fluctuation), again to rise after re-assuming the erect posture. Fatiguing marches are capable of producing a further increase of body-heat, in the rectum of one half degree and more. At night all muscular activity usually ceases, and on that account perhaps the temperature might be lower at this time than during the day; whether sleep as such has an extra-depressing influence, is not proven, though it is very probable.

The influence of MENTAL ACTIVITY upon the body-heat, though undoubted, is very much less than that of bodily exertions.

Of PHYSIOLOGICAL PROCESSES, menstruation, pregnancy and parturition also occasionally exert an influence upon the body-heat. Menstruation has the least effect; rarely, without other diseased conditions, causing a febrile temperature. In the last two months of pregnancy the vaginal temperature is increased by several tenths of degrees: in the morning 37.9°–38.35° C.; in the evening 38.1°–38.65° C. The pregnant uterus is on the average 0.15° C. warmer than the vagina, undoubtedly in consequence of the animal heat of the fœtus. During labor there is an increase of several tenths of degrees, in such a way that during the pains and immediately after them the temperature rises somewhat, but in the interval between the pains it again sinks. The daily fluctuation of the healthy state is at the same time not much altered. Immediately after giving birth a decrease of temperature frequently seems to take place, but it is soon after and during the course of the parturian month frequently slightly increased. Even if

the temperature be at first perfectly normal some puerperal disease may
still occur at a later period.

Animals and human beings become heated during coition. The maximum of this
heat does not exceed 2° C.; this increase in temperature is not in consequence of
movements; it is present in both sexes. It is the best explanation for the fatiguing
effect of coitus, for the consequently occurring hunger, etc. (WALTHER, *Med. Cen-
tralbl.*, 1864, No. 51.)

The influence of EXTERNAL COLD AND WARMTH upon bodily heat in the
healthy presents very complicated conditions. First, almost never does either
act alone upon the organism, but they are combined with some not indifferent
medium. In cold and hot baths, the effects of the water; in cold and warm
air, its degree of dampness, its movements, and its degree of pressure; in
drinks, besides the water, the other ingredients of these fluids must be con-
sidered; and it is not always possible to calculate accurately how much of
the effect is due to thermic influences and how much to these incidental
influences. The most important facts are the following: Moderate action
of cold upon the surface of the body increases the temperature of the inter-
nal parts. So the thermometer, retained in the closed axilla, rises a very
little during undressing in a cold room, also on application of a cool full,
half, or sitting bath, if continued for a short time. Application of longer
duration of moderate, but especially of intense cold, decreases the body-heat
decidedly. Warm baths, being in warm air, increase the temperature,
though only moderately. So does living in a warm climate. Cold drinks,
in sufficient quantity, diminish the body-heat, and this can be reduced about
one degree by partaking abundantly of cold water.

The KIND AND QUANTITY OF NOURISHMENT have only a very limited influence
upon the body-heat, as long as the individual is healthy. Without doubt
any increase in the production of heat induced by it is instantly compen-
sated by increased radiation of heat, and so the equilibrium is not disturbed.
A meal, especially the first in the day, appears to increase the body-heat
considerably more than the others taken in the course of the day; a late
supper also appears to be able to defer somewhat the fall of temperature.
Deprivation of nourishment only influences the temperature if health begins
to suffer in consequence. Ingestion of alcohol, according to numerous ob-
servations, reduces the temperature; strong coffee and tea increases it.

LARGE LOSSES OF BLOOD are usually followed by a decrease of temperature,
of short duration, but which is soon compensated by a new increase. After
venesection this new increase is said to exceed the previous temperature.

All fluctuations in the degree of body-heat in the healthy are, according
to what has been adduced above, almost insignificant, and certainly only
temporary; after every deviation upward or downward an effort is made in
the reversed direction. Every accidental interruption in the order of
things is instantly equalized in the healthy.

The exceeding importance of temperature-measurements to pathology is
indicated in the law, that: EVERY ONE IS SICK WHOSE TEMPERATURE IS NOT
WITHIN THE LIMITS OF HEALTH, EVEN IF HE SHOULD FEEL SUBJECTIVELY WELL
AND HEALTHY. But a normal temperature may exist even in disease.

According to this, it can be proven by a single measurement whether a
person is sick. But not only this: a single measurement frequently gives
important indication for the diagnosis and prognosis of the case. But the
latter is only made possible by a thorough acquaintance with the laws of the
course of temperature in various diseases, as taught by special pathology.

But much more complete is the insight into the conditions of a case we gain by regularly repeated measurements. It is most useful to make two observations a day, morning and evening, at about the same hour. More frequently repeated observations will give a truer and more comprehensive representation of the disease, and thereby aid the judgment in regard to some occurrences. For the state of the temperature is undoubtedly in many acute diseases the truest reflection of the general disorder of the organism. Moreover, many local disorders can be recognized by the condition of the temperature, and many complications and modifications of the usual condition can only be demonstrated by the abnormal state of the body-heat, or at least first detected through it. In the same way the condition of the temperature frequently makes it possible to judge of the intensity, and thereby of the prognosis of a case, inasmuch as the latter is often dependent upon the intensity of the fever: for by unusual height of fever and its continued duration alone, death can be produced.

The state of temperature is most practically recorded by marking with dots the different observations upon a chart divided into abscissæ and ordinatæ, and uniting these dots by lines, a curve, the TEMPERATURE or FEVER-CURVE, is produced. By means of this simple mode of representation it is exceedingly easy to keep in mind the different observations: by a single glance at this curve it is frequently possible to form a diagnosis of the case, to see the necessity of employing other methods of examination, to recognize the stage of the disease, and to predict the fatal termination.

As in all conditions, so also do we find in thermometry a gradual transition from health to disease: a sharply defined limit, a certain temperature as limit for both cannot be stated, neither as a principle nor in a given case. Between the undoubtedly normal and undoubtedly morbid figures there are only a few tenths of a degree downward, but particularly upward, of neutral ground.

In many diseased conditions the anomaly of body-heat exists in nothing but in a greater fluctuation of the temperature. Moderate influences produce more readily and more considerable deviations from the normal heat, the daily fluctuations are of larger range, the daily maximum is somewhat higher, the daily minimum somewhat lower, slight accidental disturbances of the general health induce unusual increase or decrease, though of short duration; in short, the regular temperature-curve of the healthy, which is the same day by day, is changed either permanently or at least, on more or less numerous days, in greater or smaller degree. The conditions in which this state of the body-heat is present, occur very frequently. They are not only decided slight acute and chronic diseases, but also frequently only a certain feeling of ill-health, irritability, continued fatigue, disordered digestion, etc.

Very frequently in disease the animal heat is at all times, or at least in the evenings, moderately increased, more rarely decreased, particularly in the morning. Some more considerable increases or decreases may occur during this time. This condition is present in slight acute or chronic disorders, and especially in convalescence; the temperature is frequently decreased in certain forms of insanity.

Some characteristic forms of abnormal temperature are insensibly added to these deviations, without the general condition being sufficiently well-marked by the state of the temperature. Only an essential and very characteristic as well as practically important peculiarity of the abnormal condition of the constitution, is thus expressed by the temperature.

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In a CHILL the warmth of the body is usually considerably increased; it amounts, as a rule, to 40° C. and more. But the skin of the parts of the extremities distant from the trunk (hands and forearms, feet and calves), as also a part of the face (nose, chin, ears, forehead), presents, as a rule, a more or less considerable decrease of temperature. A subjective, very severe feeling of cold is experienced. Combined with this are usually pallor of the skin, with cyanotic discoloration of the nails and other parts, automatic and convulsive movements (yawning, chattering of the teeth, trembling), and severe nausea with thirst, headache, vomiting, etc. As a rule, the chill occurs in the beginning of a febrile disease, or of an attack of fever, after it has been preceded about one-half to two hours by a gradual slow increase of the temperature of the trunk (at times very slight, at others more considerable), occasionally also by the increase of a subnormal temperature to the normal line or above it. The chill lasts, as a rule, only for a short time, about one-half to two hours, and during it the temperature of the trunk usually rises very considerably. Gradually the chill subsides, and disappears with occasional recurrence of short duration, especially after exposure, while the feeling of warmth extends to the peripheral parts which were more or less cold since the beginning of the chill, or even since the first increase of temperature. The animal heat attains its maximum occasionally at the termination of the chill, more frequently in the subsequent stage of heat. Its further course depends upon the disturbances which caused the chill; and it is worth mentioning that the sensation of cold, as well as the other symptoms of chill, are regularly entirely absent, notwithstanding a perhaps considerable and rapid decrease of temperature consecutive to the chill, even if it falls beneath the normal.

But all the subjective and most of the objective symptoms of a chill may occur without any rise of temperature, e.g., after severe irritation of sensitive nerves, after immediate introduction of toxic substances into the circulation (nervous chills); on the other hand, the temperature may under the same circumstances, which are usually present in a chill, rapidly rise, without a trace of chilly feeling appearing: rises of temperature, especially rapid ones, and symptoms of chill are therefore frequently, but not necessarily combined.

Attacks of chills occasionally occur with a falling temperature, e.g., during large hæmorrhages (chills of collapse); occasionally with very greatly increased temperature, without coolness of the peripheral parts and without any other known cause (e.g., in pyæmia). On the other hand, coolness of the periphery exists frequently without chilliness, even with increased or increasing temperature of the trunk. All this tends to show that the chill is a symptom-group, whose several parts: deviation of temperature, abnormal sensations, and other objective symptoms, do not necessarily depend one upon the other.

FEVER-HEAT depends upon increased animal heat of the body without the group of other subjective and functional phenomena, which characterize a chill. It may follow this, but can also arise directly from the normal temperature without any sign of a chill. Its intensity varies considerably. Occasionally only the increased temperature appears to be present; but most frequently other symptoms occur with it. Most remarkable are the changes in the pulse, in the secretion of urine, in respiration; the sensation of subjective heat, thirst, debility, discomfort; furthermore, functional disorders of different kinds without organic diseases: want of appetite, disordered digestion, restless sleep, fatigue, weakened psychical activity, increased irritability and sensitiveness; lastly, consumption of the tissues and de-

crease in the weight of the body. But the increased temperature and the degree of its increase are not in constant relation with any of the symptoms enumerated, although in some cases of disease its influence is unmistakable, even preponderating. On account of the incongruity of the temperature and the other disturbances, it must not be supposed that the temperature is not a criterion for judging of the constitutional state, and that its observation is unnecessary; for experience teaches that it gives a truer insight into the course of disease than any other symptom of fever, yes, even than all other symptoms combined. The distribution of fever-heat over the different parts of the body is frequently not uniform, inasmuch as the face, head, hands, are occasionally especially hot, occasionally cooler. There is, therefore, frequently a contrast between the temperature of the trunk and that of the periphery.

COLLAPSE is, as also frequently the chill, an accidental, more or less isolated condition, occurring in the course of the disease and modifying it in important points, and which, if of a certain intensity, attracts all attention for a time, and causes the main disorder to be overlooked for a while. Like chill and fever-heat it is a constitutional disorder, characterized by a disturbance of temperature, in important points the reverse of the latter, resembling the former, especially in regard to local cold, at least in peripheral parts. It is always, even if comparatively much protracted, of short duration; but it exceeds, if at all well marked, the duration of common chills. Its intensity is very variable. In the slightest degrees the patient makes no complaint; all objective symptoms, especially fever or a condition without fever, continue the same, but nose, cheeks, forehead, ears, hands, feet are frequently, without being noticed by the patient or without causing him to feel any worse, cold without extraneous influence of cold. From these slightest degrees the collapse passes, by hardly noticeable degrees, to the most intense form, in which the patient lies pale, motionless, and almost without any signs of life, similar to a corpse, icy cold over almost the whole body, with hardly perceptible pulse, hardly noticeable respiration; the skin, devoid of turgor, is usually covered with abundant cold perspiration. Disagreeable sensations, a feeling of the greatest weakness, disfigured features, sunken eyes, oppression, dizziness, fear, nausea, confused perceptions of the senses, accompany occasionally even the lower, most frequently the higher degree of collapse in a more or less well-marked manner. The most important change of temperature in the symptom-group of collapse is the LOCAL DECREASE OF ANIMAL HEAT, especially at the periphery. The temperature of the internal organs may be various: it may be normal, decreased to the lowest, but also increased to the highest degrees. During the development of the collapse the body-heat may be in a decided state of decrease or of increase, and may present any condition during its duration independently of the condition at the commencement of the collapse, especially near the lethal termination, which frequently occurs during its course if it is of excessive degree. Notwithstanding this apparent disorder and irregularity, certain conditions are present to which the collapse can be ascribed: abundant loss of heat and feebleness of the circulation, in consequence of which the peripheral losses of heat cannot be sufficiently replaced. Both conditions may become active with the various conditions of warmth in the internal parts, and still have the same effect: cooling of the periphery of the body. We accordingly distinguish collapse with high from that with low degree of body-heat.

The former is observed especially in the most intense cases of severe febrile affections,

chronic as well as more particularly acute, because the heart's activity is most weak-
ened by the unusual increase of animal heat ; it therefore frequently introduces the
agony.   Collapse with low degrees of body-heat is also frequently a collapse of agony,
as toward death the production of heat is frequently (especially in chronic diseases)
reduced to a minimum. Besides these we must also distinguish : collapse of the
definitive defervescence at the close of the febrile period of acute diseases; the remis-
sion-collapse in the remittent fever of severe acute, still more frequently chronic dis-
eases, which frequently recurs regularly, and then is usually of short duration; the
collapse in intermittent forms of fever, which may follow the chill, or the fever-stage,
or the stage of the subsiding fever in pernicious cases ; finally, the incidence-collapse
occurring accidentally in any stage of disease.   Collapses occur in persons apparently
perfectly healthy, as also in those already diseased, particularly the seriously diseased
and considerably weakened by disease, especially in sensitive originally feeble per-
sons, as women, children, aged persons, anæmic individuals, drunkards.   Their occa-
sional causes are : over-exertion of physical as well as mental form, e.g., sudden
emotional shocks, severe diarrhœas, eating large quantities of indigestible food, severe
vomiting, profound narcosis, intense pains, even sitting in bed, or a normal passage
from the bowels ; certain diseased conditions, as perforation of pleura and peritoneum,
intoxications and infectious, especially cholera ; lastly, considerable natural or arti-
ficial losses of blood.   The body-heat falls in these collapses almost regularly, fre-
quently in a very dangerous degree ; not rarely they induce unexpected and rapid
appearance of agony.   Their duration in convalescents is very various : occasionally
very short, minutes or a few hours, occasionally they last one or even several days.

OF THE SEVERAL POINTS WHICH ARE OF IMPORTANCE IN REGARD TO THE
CONDITION OF BODY-HEAT IN DISEASE, the following need mentioning : local
deviations of temperature, the possible maximum and minimum degrees, the
height of the fever and the temperature-values in general in their different
relations, the daily fluctuations, the types of fever ; lastly, the general course
of the temperature in febrile diseases.

The deviations from the normal temperature in the sick are partly local
and restricted to some portions of the body, partly general and more or
less equally distributed over the entire body. This statement is not per-
fectly true, inasmuch as in evidently general anomalies more moderate local
excesses are frequent, and with sufficiently large local deviation the gen-
eral temperature also shows fluctuations; still it can be retained as useful in
practice.

An ABNORMALLY INCREASED LOCAL TEMPERATURE has been observed,
especially in inflammations and in paralyses. As a rule, measurements of
inflamed parts, which have been mainly taken in wounds, show a lower tem-
perature than the rectum or the axilla ; still some exceptions are adduced, to
the disadvantage of at least the latter. But distinct differences were shown
between the figures thus obtained and the temperature of the corresponding
parts of the other half of the body, or of the same parts in a healthy condi-
tion.   In paralyses, especially hemiplegia, the palsied limbs are usually at
first somewhat warmer, rarely are both sides equal, almost never is the
healthy one warmer.   Cure of the paralysis brings back the thermometric
equilibrium, development of paralytic atrophy causes a lower temperature
than that of the healthy side.   One-sided increase also occurs in hysterical
persons.   Partial decrease of body-heat frequently exists in mortified,
œdematous, palsied parts of the body.

M. HUPPERT (Arch. d. Heilk., 1873. XIV., p. 73) proved by careful examinations
the influence of the condition of inflammation after an operation for hydrocele upon
both local and general temperatures.

By far the most important are the DEVIATIONS OF THE GENERAL TEMPERA-
TURE IN DISEASE.

The possible MINIMUM of animal heat in a sick person as well as the possible maximum cannot be positively stated, and is certainly very different in each individual.

The MAXIMUM found in a living person (case of tetanus during the agony) was 44.75° C. in the axilla; an increase above 42° in convalescents is very rare, only few examples are recorded in literature.* Errors of observation most easily occur with low degrees; and those parts permitting the measurement, even if well protected, cannot in unusually low degrees of heat be taken as an index of the temperature of the internal organs. The lowest values, to about 25° C., have been observed near death (but yet even several days before the end), certainly under partly quite abnormal external circumstances, in the insane, who seem to have a greater tendency to low temperatures than those mentally healthy. In the latter a fall to about 33° C. in the axilla occurs exceedingly rarely.

PETER (*Gaz. hebd.*, 1872, No. 4 et 6) observed in a woman 38 years of age, who had spent a winter night insensible and drunk in the open air, 26° C. in the vagina. She recovered, the temperature rising within six hours 10.3°. BOURNEVILLE (*Le Mour. méd.*, 1872, No. 9) found in a man 45 years old, who had been exposed naked to the cold, 27.4° C.; death occurred after 9 hours with 36.2° C. He also observed in uræmia before death a decrease to 28.1° C. LÖWENHARDT (*Allg. Z. f. Psych.*, XXV., p. 685) found in the insane, who lost more warmth on account of their condition (uncleanliness, tendency to exposure), during the latter period of life very low degrees, fluctuations for days between 25° and 31° C., at death a fall to 23.75° C.

The simplest division of grades of temperature which come under observation in the sick, is into NORMAL, SUB-NORMAL, and into SUPER-NORMAL or FEBRILE.

NORMAL GRADES occur in many, especially patients having chronic diseases, and in them the temperature may, as it fluctuates between the normal limits, present sometimes the same course as in the healthy, sometimes remain nearer to the higher or lower limit, sometimes show an irregular condition. At any rate, the tendency to excessive temperature which characterizes the sick, exists here also.

SUB-NORMAL temperatures appear exceptionally during a longer period usually only at the time of the subsidence of fever, as excessive temperature decreases, or in the agony; also under particular influences, e.g., bleeding, collapse-conditions. It is well to distinguish sub-normal values (about 35° C. for the axilla-measurements) in the milder states, and collapse-temperatures (under 35° C.) in conditions of collapse.

By far most frequently SUPER-NORMAL values exist in the sick. It is best to term axilla-temperatures up to 38.0° C. as HIGH-NORMAL; from 38.1°–38.5° C. as NON-FEBRILE; from 38.6°–39.0° C. as SLIGHTLY FEBRILE; from 39°–40° C. as FEBRILE; over 40° C. as HIGH-FEBRILE; over 41° to 41.5° C. as HYPERPYRETIC. (The values for the rectum and vagina are, as before mentioned, about half a degree higher.)

Temperatures under 38.1° C. are to be designated as HIGH-NORMAL or NON-FEBRILE, because they frequently occur in decidedly non-feverish patients. Even healthy persons with greater sensitiveness to external influences, especially children, and therefore also convalescents, show such an increase of temperature, e.g., not rarely after an abundant meal, after unusual mus-

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* A truly extraordinary case of recovery after much higher temperature than ever before observed is related at length in the London *Lancet*, March 6, 1875, by MR. TEALE. In this patient injury to the spine caused hyperpyrexia, lasting many weeks, the maximum being 50° C. For further details see SEGUIN, *On Thermometry*, N. Y., 1876, p. 220.—[ED.]

cular exertion; but it arises with more difficulty, the stronger and the more capable of resistance the organism is, the more firmly health has been re-established. In the sick it depends upon co-existing circumstances whether the existence of fever is to be accepted or not. We would decide for the slightest degree of fever sooner, if the suspicious high-normal value is observed in the morning, before any food has been taken, after a long rest in bed, than if it occur under the reverse circumstances.

All axillary temperatures above 38.0° C. are at the least suspicious, and a few tenths more prove with certainty that a slight fever exists. To establish whether in a certain case moderate, considerable or intense fever exists, it is necessary to note particularly the hour of the observation. By equal temperatures the various figures are the more important, and speak the more for a considerable intensity of the fever, the earlier they are observed in the morning, *i.e.*, at a time when a subsidence of the fever usually occurs. Slight maladies are generally characterized by slightly febrile and febrile temperature-values, the latter at least in the hours of evening, while the enrves of severe cases and of serious diseases generally show these degrees of heat, even at the time of subsidence of fever; and give, besides, especially in the evening, the high-febrile values. In a very severe fever the morning temperatures also are high-febrile.

HYPERPYRETIC temperatures are such as considerably exceed even the high-febrile, and which are by no means to be merely viewed as an expression of a very intense fever. Their cause is undoubtedly in other circumstances; they mainly depend either upon infecting influences, or are a symptom of beginning and rapidly progressing general paralysis. In the latter case, they occasionally occur at the termination of diseases in whose course the febrile element was absent or only slightly developed, in the form of a very intense increase of short duration.

Undoubtedly dependent upon the specific influence of infection are the hyperpyretic temperatures, or such extraordinarily high ones bordering on them (41°–42° C. and more), very commonly observed in paroxysms of malarial forms, frequently in the course of relapsing fever. If such extreme values in these diseases do not predict danger, or at least no especial danger, this is not the case if they occur in other diseases, as typhoid fever, scarlatina, measles, small-pox, pneumonia, puerperal fever, pyæmia, malignant rheumatism, meningitis of the convexity, etc., for here they frequently precede the period which terminates in agony. If in these cases the temperature rises to 41.5° C. the chance for recovery is very small; at 41.75° C. death is almost certain.

Premonitory symptoms of paralysis are the suddenly and unexpectedly occurring hyperpyretic temperatures during a non-febrile or slightly febrile course, especially in diseases of the central nervous system, in tetanus, epilepsy, tumors, injuries, etc. The temperature may here rise enormously in a few hours, to 44° C. and more.

The DIAGNOSTIC VALUE of the absolute height of a certain temperature by itself is very slight. The formation of the PROGNOSIS is more possible, at least, in abnormally high or low temperature values. These are symptoms of approaching death, or at least of decided danger, with the restriction that in certain diseases (*vide supra*) even unusually high figures may still admit of hope for a favorable termination. Besides, the temperatures usually attained are different in some diseases: *e.g.*, a height, which is a rule in one affection, forms a dangerous exception in another.

The INDIVIDUALITY of the patient must moreover be kept in mind when judging the result of a measurement.

In CHILDREN the body-heat in disease has in general the same signification as in adults, but it presents frequently a more sudden change of tem-

perature and on the average a higher degree than in older persons, at least in simple catarrhal and inflammatory disorders. The temperature changes more rapidly after incidental influences, and reacts upon them more considerably. To infancy especially, therefore, ephemeral febrile attacks without any important cause belong. A high-febrile temperature is not by far of the same importance in them as in adults, although it requires the most careful observation; and where adults, e.g., in convalescence, show a normal temperature, we frequently find in children a moderate increase. Therefore no sudden conclusions should be drawn from the first observation in children.

SENILE PERSONS and those in advanced age frequently present, on the contrary, in disease temperatures which are a half to a whole degree or still less than the average height which is reached in the same disorder in younger individuals; the low temperature-values of collapse also occur more frequently in the former than in the latter. Already at the age between forty and fifty, and in exceptional cases even before forty, remarkably low values are occasionally found. If this is not taken into consideration the seemingly moderate temperature may easily misguide in regard to the form and danger of the disease, especially at the first measurement and before a certain diagnosis has been arrived at. Febrile affections in senile persons are therefore never to be lightly treated.

Many WOMEN AND IRRITABLE INDIVIDUALS GENERALLY in middle age show occasionally a similar condition of temperature as children.

The TIME OF DAY at which the observations are made must be considered in every application of the result of the measurement. For never does the body-heat of a sick person remain during a period of twenty-four hours at the same point, and observations which record a certain temperature as lasting throughout the day are certainly false.

The DAILY FLUCTUATIONS are in the sick usually more extensive than in the healthy. It is quite common to find that the temperature of a patient changes by $1-1\frac{1}{2}$ degrees in the course of a day, and it may change for far more considerable values (6–8 degrees); it may also present a different record on different days in the same patient, and also change in different patients with the same disease. Minute fluctuations, with high temperature, indicate a considerable, moderate fluctuation with lower temperature, a moderate intensity of fever. Very considerable fluctuations occur with an irregular course of fever, as well as with complications.

To get a clear representation of the condition of the fever-temperature in the course of a period of twenty-four hours, observations should be made as frequently as possible; if possible with a thermometer continuously retained in its position, and the separate observations, recorded upon a chart (vide supra), united by means of a curve. This is the curve of the daily fluctuation.

Four stages are distinguished in the daily fluctuation. The stage in which the temperature rises considerably, is called INCREASE, EXACERBATION, ASCENSION; that in which it sinks, DECREASE, REMISSION, period of subsidence, DESCENSION. Between the two is the curve-point, the HEIGHT OF EXACERBATION, whose highest point is called the DAILY MAXIMUM. The distance of the excursion between the daily maximum and daily minimum is the DAILY DIFFERENCE. The duration of each of the above-mentioned four periods, their extension, may differ very greatly in different patients and in the different stages of a disease. The extension of these periods must be considered in deciding the intensity of the fever, as well as the height of

each separate temperature-value. In considerable fever the exacerbation, and especially the exacerbation-height, the point of the curve, possess considerable extension; while in inconsiderable fever the extension of these periods is small, and the prolongation of the remission, especially the depth of the remission, is increased.

The regular course of the daily fluctuation in fever of moderate intensity is about the following. In the first hours of forenoon, at about 9 o'clock or somewhat earlier, the exacerbation (the increase of the temperature) usually begins, and lasts until the afternoon. From now until evening, therefore for a period of 3–4 hours, the height of the exacerbation exists, and terminates at 7 or 8 o'clock in decided falling of the temperature, the remission. In the early hours of morning, perhaps at 5 or probably only at 6 or 7 o'clock, the depth of the remission is attained. (A DAY OF DISEASE is usually calculated not from midnight to midnight, but from one remission-depth to the next. Some impractically place in several diseases of sudden origin the beginning of the day of disease at the hour of the invasion, without reference to the daily fluctuation.) In excessive fever the point of the curve is occasionally already attained in the late hours of the forenoon and quite commonly at noon, and only left in the late hours of evening, very frequently only at midnight; the duration of the remission depth is then, of course, very short. In slight fever the latter on the contrary reaches frequently from early morning to noon or even afternoon; in the evening a short increase appears with an acute angle of the curve late in the evening or at beginning of the night.

The course of the temperature within the several stages of the daily curve may be very different. If very frequent measurements are taken, an interrupted increase during the exacerbation is not rarely observed, interrupted by the temperature remaining stationary or even falling slightly. More frequently yet a discontinuity of the falling in the remission occurs; occasionally the temperature remains here at exactly or almost exactly the same level for several quarters of an hour (so-called terrace-formation), until suddenly the decrease continues. This occurs especially in slow ascension and descension. Still more variable and important is the condition of the apex of the curve. In the simplest case the temperature at its level slowly rises and sinks to a very moderate degree,—this is rare, and occurs almost only in very slight fever. Very commonly with it appear accidental exacerbations and remissions, i.e., fluctuations of temperature, which do not by far attain to the morning remission-depth, often only amount to a few tenths of a degree, but nevertheless are much more considerable than the above-mentioned unimportant fluctuations. The daily curve therefore becomes two or three pointed. In the latter case the first point is attained at noon, the second in the early hours of evening, the third at midnight or in the second half of the night (if it occur here it belongs more to the second remission and is only an interruption of it); in the former case the two points occur at noon and evening, or at evening and night. More than three apices upon the daily curve, which are separated by distinct decreases (accidental remissions), are rarely found; but two or three points are according to the rule. The remission depth is usually simple; it commonly shows inconsiderable fluctuations, occasionally for a long period an evenly low state. Only rarely is the third accidental exacerbation, which ought really to close the point of the curve, and which is occasionally regularly removed into the remission, noticeable as a slight increase at its termination, i.e., in the closest proximity to the remission-depth. The formation of accidental remissions (and consequently also of preceding accidental exacerbations) in a fever of high degree is to be accepted as a favorable symptom, particularly when the incision of the curve is very deep. In this case it sometimes descends to the value of the remission depth, and the daily curve appears, instead of with two or three points, cleft or doubly cleft. The fever-waste must naturally be less in an interrupted fever than in a continuous one.

In every regular fever of acute disease we find morning remissions, evening exacerbations; considerable deviations from this indicate a perhaps obscure disturbance of the course, and cause others to be expected. In chronic febrile diseases the course of the fever is very frequently the same—frequently two pointed exacerbations are also found—but not rarely the time of exacerbation and remission is gradually changed, and may even be completely reversed: the exacerbation-height appears in the morning, the remission-depth in the evening. In such a condition, usually, an exceedingly irregular course of fever is at hand.

The DAILY DIFFERENCE, or the extent of the excursion between the daily maximum and daily minimum, may be variously large, but may also possess with the same length different importance, according how high or low the daily average, or average temperature of the fever-period for twenty-four hours is, whether it rises or sinks.

Small daily differences—with considerable fever are generally symptoms that the disease is still in an early period, or that complications exist. The occurrence of remissions in the height of a disease almost always indicates an improvement, or even a transition into the stage of convalescence. The continued occurrence of remissions, especially the increase of the daily difference, proves the progress of convalescence; while the cessation of remissions with a continued febrile condition without decrease of the daily average indicates a relapse, or a complication. Large differences, produced by the remission-values becoming sub-normal, may be favorable or indifferent, or may indicate danger; increasing exacerbation-values are to be regarded as decidedly unfavorable in such a condition.

By TYPE OF FEVER, the kind and mode of the course of the fever on several consecutive days is understood. If on them the daily difference is very inconsiderable (at the most .5° C.), the fever is called continued, *febris continua*; if the difference is somewhat greater, the fever is designated *febris subcontinua*; if it amounts to more than one degree, it is remittent, *febris remittens*. In these the exacerbation and remission usually have the above-described characteristic course.

The CONTINUOUS and sub-continuous fever-types occur almost only with high temperatures and never continue long with them. They occur in all extensive inflammatory processes, also in the second half of the first, and a part of the second week of abdominal typhus (typhoid fever), in severe cases of scarlatina and small-pox, in exanthematous typhus. The more marked they are by high temperatures, the more serious is the case. If in pneumonia or other inflammations an intense fever (40–41° C.) retains this type for only a few days, in typhoid fever for 1–1½ weeks, life is very seriously endangered. Accompanied by lower temperatures, the continuous fever-type is endured for a longer period, *e.g.*, in acute rheumatism, pleuritis, local peritonitis. The usual type is the REMITTENT. It occurs especially in the later stage of typhoid fever, in the lighter cases even in the second week, in the severe cases later if the course be favorable. It frequently occurs in bronchial and intestinal catarrh, in catarrhal pneumonia, tuberculosis and other diseases. With the same evening temperatures it is much more readily and longer endured than the continuous type.

Another fever-type is the INTERMITTENT (*febris intermittens*). It is characterized by intervals, occurring between the periods of high temperatures, of normal or sub-normal values, and therefore a period of fever (fever-attack paroxysm,) and a period without fever (apyrexia) alternate. It occurs most clearly in the intermittent fever which arises from the influence of malaria.

The febrile paroxysm arises and disappears very rapidly, and therefore is but of very short duration. We distinguish in it the ascension, which, accompanied usually by chills, is continuous, and completed frequently in 1–2 hours; the height of the attack, which with slight fluctuations runs its course similarly to an exacerbation-apex, and the descension, which may continue for 8–10 hours and usually occurs typically in the form of terraces. In intermittent fever such attacks occur daily, the apyrexia therefore lasting scarcely half a day—QUOTIDIAN RHYTHM; or every second day with an apyrexia of 36 hours—TERTIAN RHYTHM; and so on. More rarely the rhythm is irregular. But the term intermittent fever is also used in different other acute and chronic maladies, if between the attacks a perfectly feverless interval, even if only of short duration, occurs. (Some designate such a fever as strongly remittent.) Such an intermittent type occurs occasionally very distinctly in the second half of typhoid

fever, in which case usually its transition from the remittent type can be very nicely observed; also in pyæmia, puerperal fever, tuberculosis, in suppurations generally; similarly also in affections of the biliary passages. But certainly it is not so characteristic in all these conditions as in malarial intermittent fever. The danger of intermittent fever generally, exclusive of the co-existing local disorders, is less than that of remittent or continuous fever, as the organism can be somewhat restored during the apyrexia.

A rudimentary fever-form is the EPHEMERAL. Its short duration is its characteristic, amounting very frequently only to a few hours or one day, occasionally two days, rarely more (*ephemera protracta*). The frequently considerably increased temperature (to 40.5° C. and more) is occasionally the only symptom of a constitutional disorder. Such a febrile paroxysm, similar to a paroxysm of the intermittent type, arises usually in sensitive individuals, as children, convalescents, women, from inconsiderable causes, which would not produce any disorder of the constitution in robust persons.

FEBRILE DISEASES exhibit a very great variety in the degrees of body-heat. Nevertheless certain rules can be recognized in spite of differences, and yet these differences present most important points for the recognition of the several diseases. First we must separate acute from chronic diseases.

In ACUTE FEBRILE AFFECTIONS the temperature remains, (1) at least until the maximum of the development has been passed, either constantly above the normal or falls only occasionally and quite momentarily to the normal or below it, under the influence of incidental circumstances: LASTING CONTINUOUS FEVERS. Or (2) the increased body-heat is interrupted once or oftener by febrile (normal or sub-, or also only high-normal) temperatures: INTERMITTENT and RELAPSING FEVER. Each attack of fever has a course here more or less like that of a continuous fever of short duration. The temperature-increase is sometimes dependent mainly upon the disease, at least in a part of its course; sometimes more incidental circumstances and especially upon the intensity of the disorder, as also upon individual conditions. To diseases of the first class belong most of the decidedly typical forms, also a number of those which are approximatively typical. All others, as well as the atypical fevers, belong to the second class, with more accidental temperature-increase.

In typical diseases a certain course of the body-heat accords with the certain course of the disease. In contradistinction to these the course of the affection generally, in atypical diseases as well as the course of the temperature, lacks regularity. The transition is formed by the more or less approximatively typical forms of disease. (*Vide* p. 14.)

The COURSE OF THE BODY-HEAT in febrile diseases is determined: (1) by the kind of disease, especially in typical maladies: the clearer and less complicated the disease appears in a previously healthy individual, the more typically, so to say, the more normally the normal temperature of the affection runs its course; (2) by their intensity, even in typical affections: (3) by individual conditions, more particularly that of age; (4) by incidental circumstances, especially also therapeutical influences and complications (primary and secondary origin of the disease). It is divided into a number of periods, which, differing in their significance, present a changing picture; and while they are in some diseases and in many single cases distinctly separated, in others they merge one into the other. The following periods are distinguished: (1) the period of the development of the fever: pyrogenetic stage, INITIAL STAGE; (2) the period of the fully formed fever:

FASTIGIUM; (3) that of the decidedly subsiding fever: the period of SUBSI-DENCE, DEFERVESCENCE. To these three also follow (4) the period of CON-VALESCENCE, and (5) the period of the transition to the lethal termination: PRE-MORTAL PERIOD.

The INITIAL STAGE extends from the commencement of the affection until the lowest average temperature, characteristic of the fastigium for the special disease, has been attained. To this height the temperature rises more or less rapidly, by continuous or by discontinuous ascension. If the increase occur rapidly, it is usually continuous, not at all or scarcely interrupted by decrease, and occupies at the most twenty-four hours, very frequently only half that time, and even less.

Thus it is in measles, scarlatina, small-pox. primary pneumonia, meningitis of the convexity, *febris recurrens*, amygdalitis. erysipelas. The ascension of the temperature occurs slowly, and then always discontinuously in typhoid fever, in exanthematous typhus, catarrhal pneumonia, catarrhs, articular rheumatism, and in others. It runs its course most regularly and most typically in typhoid fever, in which the temperature is higher every consecutive day at the same hour, as ever larger increases occur in the evening and moderate decreases in the morning. In many cases the development of the usually moderate fever is much slower. These are partly such in which the development of the fever follows the local disorder. not as in those already described, in which it precedes, or in which an uninterrupted fever is only decidedly developed with the increase of the local disorder.

The period of the FASTIGIUM, the complete development of the fever, presents much more considerable differences. This is owing to the exceedingly great variety of possible circumstances.

First, the height of the MAXIMUM TEMPERATURE, the highest point which the temperature attains during the disease, is very various in different cases. It is partly determined by the form of the disease, partly by the intensity of the case, but very frequently only by incidental circumstances, by which an unusual single increase is induced. It may, under those circumstances, be of subordinate interest, but certainly becomes very important, if it attains an enormous height, *e.g.*, 42° C. and more; a height which is but very rarely consistent with prolonged continuance of life. But it is most useful to know the limiting figures of the numerous severe and intense cases accompanied by continuous high fever (*febris continua continens*), which yet possess a normal course not influenced by incidental circumstances. This is important in relation to diagnosis and prognosis, as frequently much depends upon several tenths more or less at the higher limit.

Only under peculiar circumstances, especially in regard to diagnosis, the knowledge of the limiting figures of the maximum temperature in characteristic slight cases is important, *e.g.*, in typhoid fever, in which, in a characteristic course, it hardly falls below 39.6 C. A special enumeration of numerous numbers would lead too far into the field of special pathology, and therefore it is only remarked that for serious cases of most infectious diseases (excepting relapsing fever, which rises higher) about 40.5 C. forms the average maximum temperature; that in the interrupted fastigium of intermittent fever 41 C., and somewhat more in the paroxysms, is very frequently attained; as also that most local diseases in severe cases fluctuate at about 40 C.

The most valuable elements for the judgment of a case are derived from the entire course of the temperature of the fastigium. This course may be either acme-like, or continuous, or discontinuous.

In the ACME-LIKE course only once, slowly or more rapidly, an apex is

attained, and after a short duration of the fastigium (rarely, and then usually with some fluctuations, more than a day), and again departed from either by means of a fall of temperature, which leads to recovery, or by the agony.

The CONTINUOUS COURSE consists of a maintenance upon a certain average height, with characteristic development of the daily exacerbations and remissions, but in which the latter cannot fall beneath the usual fever-height, nor possess an unusually long duration.

This course is not only present in all severe diseases, even with complications, when these do not, as *e.g.* hæmorrhages, act depressingly upon the temperature, but also in many slighter diseases. Examples of this are the third and fourth days of typhoid fever, exanthematous typhus, the prodromal stage of small-pox, scarlatina in its beginning, measles in its eruptive stage, etc. While in these affections a certain continuity of the course is normal, and, as long as the high temperature does not last unusually long nor attain unusual heights, it does not occasion any fear ; it is to be considered an unfavorable symptom if diseases which, as a rule, have a discontinuous temperature-course, present a continuous one.

TRANSITION-FORMS to the DISCONTINUOUS COURSE occur frequently, especially after long duration of the continuous type, and in favorably terminating disorders. First, by the remissions becoming day by day always longer, and then by unusually large but very transient falls of temperature, recurring several times, or from time to time.

They are frequently noticed, in an otherwise perfectly continuous course of temperature and often also in a not intensive course, as unexpected occurrences of seemingly favorably import, in the beginning of the fastigium as well as later, usually without any influence on the further course of the disease, occasionally in consequence of therapeutic interferences. Where they occur spontaneously, and as usual attain quite or almost the normal, they may give the appearance as though the critical termination of the fever-course had arrived (PSEUDO-CRISIS). But then, besides the knowledge of the fact that pseudo-crises occur, the close observation of the local symptoms especially prevents the false interpretation. Examples of pseudo-crises are seen in many cases of scarlatina, small-pox, pneumonia, relapsing fever, erysipelas, etc.

DISCONTINUOUS is the course in the large majority of diseases, considerable fluctuations occurring within one day, frequently also differences in the course on different consecutive days. With a regular alternation in the beginning of exacerbations and remissions, and considerable daily differences (*febris continua remittens*), the fever may continue in the same way for a month and more, according to the intensity of the local symptoms and the height of the exacerbation-maxima. But more frequently (as after an originally regular course in complicated cases which become anomalous from other causes, as also in certain disorders (for example pyæmia) from the beginning) the discontinuous course shows more or less considerable irregularities. These consist of irregularly occurring exacerbations and remission on the separate days, as also of unequal and changing height of the maxima and minima, of intercurrent spontaneous large decreases of temperature, without a consequent favorable termination, as also of intercurrent increases and collapses. Frequently the irregularity is complicated, and if considerable irregularities of the course have once begun, it is usually noticeable that the disturbed type never again completely resumes its former condition. Occasionally completely irregular fluctuations of the temperature occur, probably also occasionally even a change from a continuous to a discontinuous course.

Examples are suppurative fever, the fever in catarrhal pneumonia, pleuritis, rheumatism, trichinosis, *erysipelas migrans*, intestinal catarrh, etc.

The direction of the discontinuous temperature-course may be various: ascending or descending; or the temperature may remain at the same height; quite commonly these different directions follow one another. The ascending direction may consist of an equable increase of exacerbation and remission-values, or of an approximation of the remittent type to the continuous, the latter alone increasing; the descending direction is characterized by the reverse conditions. A reversal of the direction of the fastigium occurs gradually, or suddenly and sharply, without the maintenance of an equal character for even a short time, and is often preceded by irregularities of short duration. Perfect regularity of the change of exacerbations and remissions, according to time and height, is rare (at the most typhoid fever forms an exception); at any rate, very remarkable causes are not necessary in case of great tendency to irregularity to make the course irregular. Complications produce commonly, and thus also make the prognosis more unfavorable, an approximation to the continuous temperature-course; if, on the contrary, the temperature approximates during the remissions to the normal, while it does not or at least only slightly exceeds in the exacerbation-period the limit of a moderate fever-heat, the case may be designated mild and advancing toward convalescence, if, excluding the fever, the local disorder does not indicate danger.

The duration of the fastigium in the discontinuous type is on the average longer than in the continuous, and depends very much upon the kind of local disorder, and also especially upon the intensity of the case. Short duration in recovering cases is favorable, long duration unfavorable.

Occasionally the fastigium in a disease is double or multiple: as in typhoid fever with successive deposits, in variola (prodromal and suppurative fever), relapsing fever, in some pneumonias (relapsing and intermittent form); also in facial erysipelas, pyæmia, etc. Frequently a different type exists in the several fastigia; it is unfavorable if the later ones show the continuous type.

The TERMINATION OF THE FASTIGIUM is sometimes distinctly, sometimes indistinctly limited. With accuracy it can only be ascertained by frequent measurements. It concludes most suddenly, if after an usual and then most frequently a short course, there follow a short increase occasionally to a considerable height, before the transition into defervescence, the so-called *perturbatio critica;* most frequently it merges into the beginning of defervescence, if this be preceded by a gradual decrease of temperature (*stadium decrementi*). In a fastigium of longer duration, especially in a regular continuous or discontinuous type, a variably long period of irresolution with irregular fluctuations of temperature, and occasionally even with intercurrent collapses, is likely to occur between the fastigium and defervescence, the so-called AMPHIBOLIC STAGE. In recovering cases the temperature of this stage usually remains at a moderate height; if excessive values are attained, abnormally high as well as abnormally low ones, the termination is doubtful, and transition into the pro-agonic stage not rare.

During the fastigium the temperature can be influenced more or less readily by processes within the organism, or by artificial influences bearing upon it, to the advantage or detriment of the patient. Disadvantageous are those influences which are capable of producing an increase of the fever, as mental excitement, bodily exertion, and muscular exertions generally, being too warm, errors of diet, constipation,

and other unfavorable processes. A decrease of the heightened temperature is induced by spontaneous and artificially produced haemorrhages, by abundant defecation and perspiration; also by vomiting, inanition; occasionally also by sleep, by sufficient application of cold; lastly, by incorporation of a number of medicaments (antipyretics), of which are to be especially mentioned: calomel, digitalis, veratrum, quinia, laxative salts. It is not decidedly and always advantageous if the temperature moderate, particularly below a certain limit; and therefore medical knowledge and experience must note the appropriate cases and the most appropriate methods, as well as the right time for the reduction of the fever. But the certainty and the degree of the effect is by no means the same in all cases with the same course of temperature; on the contrary, the response to these influences (undoubtedly on account of the different intensity of the fever, notwithstanding the same temperature) is very different. So, *e.g.*, digitalis, cold baths, calomel, etc., act upon light and moderate fevers disproportionately more than upon considerable temperatures with intense local processes. Readily influenced temperatures occur more frequently in children and in the weak than in robust adults, more frequently in the *stadium decrementi* than in the *st. incrementi;* more frequently at the time of the daily remission than that of the daily exacerbation.

DURING THE PROCESS OF RECOVERY the course of the temperature is various, and certainly influenced by the kind and mode of the convalescence, although not quite determined by it alone. Undoubtedly the apparatuses, by whose activity a certain form is assigned to the deviations of temperature, possess so much independence, that they are able to influence the mode of their return to the normal. This therefore occurs in many diseases in a regular and certain way, without our being able to recognize the true reason of the differences. Although the facility or difficulty of reparation of the local disorder may have the most important influence (frequently enough the decisive fall of fever occurs when it has ceased to extend), it is not always alone the determining. By experience it is proven, that, notwithstanding the local disorder be evidently on the path of recovery, and no other new affection be demonstrable, still the fever continues in a certain independent way, and the mode of convalescence characteristic of the disease is changed.

A period of INSUFFICIENT DECREASE, *stadium decrementi*, precedes in some cases the decided decrease of temperature which leads to the normal. It either follows the fastigium directly, or only after an intercurrent short increase between it and the former. Its duration is generally short, and amounts at the most to a couple of days; it may so gradually change into the actual decrease of defervescence, that the beginning of the latter cannot be positively determined. The *stadium decrementi* is distinguished from the amphibolic stage by the non-occurrence of new considerable increases of temperature, as an unfavorable symptom. The preparatory decrease may last from half a day to an entire day, rarely more. It consists frequently only in the non-appearance, or the more moderate development of the usual evening exacerbation, so that the morning temperature-height exists almost continuously, or of a larger morning remission with equally large evening exacerbation, or of a decrease of both.

In the PERIOD OF DEFERVESCENCE, or subsidence of fever, the increased temperature of the fastigium, or at least that of the *stadium decrementi*, returns to the normal. It either occurs rapidly: rapid defervescence, CRISIS, so that it is completed in a few, at the most 36 hours, the temperature falling during that time 2°–5° C., and even more, and reaching the normal, or even sinking below it. Or, it occurs more slowly during several days, or one week and more: LYSIS. The protracted crisis must be accepted as an intervening form, in which the defervescence is completed in about 3 days; it is particularly observed in cases of disease whose normal form of defervescence is the crisis.

If the crisis is completed in 12–24 hours or (not frequently) in a shorter time, a continuous decrease of temperature is observed by rare measurements, by very frequent ones a more or less terrace-like decrease. In long duration, but particularly in protracted crisis, small intercurrent increases, which occur at the time of the main, or also of the incidental exacerbations of the daily fluctuation, and which undoubtedly possess their signification, are common phenomena; and at least the decrease in the remission-period of the daily fluctuation (at night) occurs more rapidly than in the exacerbation-period (in the afternoon). Frequently, particularly if before the crisis the temperature has attained an unusual height and then fallen rapidly, or if shortly before there appeared influences depressing the temperature, it happens that the body-heat falls far beneath the normal, to 36° C. and lower; not rarely light collapse-symptoms are developed. Such an excessive decrease gives no guaranty that a new increase will not follow (similarly to a pseudo-crisis), and only after 24 hours have passed without its occurrence is defervescence assured. Generally those diseases defervesce rapidly which show in the initial period a rapid increase of temperature, and which take a normal uncomplicated course. Most remarkable, most constant and most rapid is the crisis in relapsing fever, in which it may descend 5°–6° C. within a few hours; it is, moreover, the rule in croupous pneumonia, in normal measles, and in the eruptive fever of small-pox, frequently in erysipelas, *angina tonsillaris*, and in ephemeral fever.

LYSIS either occurs in the form of a slow, but mainly continuous decrease of temperature, which falls a little less from morning to evening than during the night, or remains stationary, or even again rises slightly. The decrease may occupy 4–8 days, *e.g.*, in scarlatina and in exanthematous typhus. Or the lysis has a remittent course, the daily maxima and minima approximating more and more the normal, now in equal, then in unequal stages (so that first the remission-values increase, until they attain the normal, and then only the exacerbation-maxima decrease), or by the development of a mixed type. Interruptions of the regular decrease are extremely frequent. Remitting lysis is characteristic of typhoid fever; it appears frequently in catarrhs, and in the suppurative fever of small-pox; also in pleuritis, peritonitis, etc., as also in complicated cases of scarlatina and measles.

During the PERIOD OF CONVALESCENCE the temperature returns to the normal degree and remains there permanently. Every deviation from this course, as it occurs especially in the beginning of convalescence, indicates a disturbance of the process of recovery, or the occurrence of a new disorder.

The temperature usually does not immediately become perfectly normal after the close of defervescence. Frequently it attains sub-normal, occasionally quite low values (to 35° C.), and there remains stationary, with fluctuations, sometimes for several days. This occurs particularly in critical defervescence. But occasionally it rises yet for a time regularly at every exacerbation-time to sub-febrile values. Not rarely the evening temperature is a little supra-normal, but the morning and especially the night temperature are sub-normal, the daily difference therefore increased. At other times this is decreased. Commonly, perfectly normal temperature sets in under such irregularities, gradually, and at the latest in the course of 1–2 weeks, especially with respect to the daily fluctuation of the healthy type, if particular circumstances do not sustain the continuance of anomalies.

The temperature of the convalescent reacts more readily than that of a healthy person to extraneous influences: by a bath, by numerous meals, by muscular exertions even of an inconsiderable degree; by leaving the bed or room it is usually changed, most frequently increased, commonly for a short, occasionally for a longer period. If such increases are considerable, if they reach into the febrile degrees, they indicate a more serious disturbance, and call earnestly for renewed precaution. They are frequently the first symptom of a relapse, but occasionally have only the importance of a simple fever-collapse. After a disease of long duration the temperature of convalescence is generally more excitable than after disorders having a short

febrile course: *e.g.*, it is more frequently disturbed after typhoid fever than after pneumonia or erysipelas. Nevertheless the kind of disease is also in a high degree determining.

The FATAL TERMINATION is not rarely preceded by symptoms of variable duration, and in great part of an unfavorable kind. They must not be judged only by the condition of the body-heat; but the other symptoms must also always be consulted, especially the frequency of the pulse and the signs of collapse, so as not to be deceived by apparent moderations. The temperature of the internal parts, as ascertained in the usual places of measurement, is in various conditions. In general it has an extraordinary tendency to the greatest irregularities and fluctuations: whichever occur, it fluctuates occasionally, so to say, without rule; collapse-temperatures alternate in short periods (not even 24 hours) with the highest febrile degrees. Occasionally, nevertheless, the influence of the daily fluctuation is shown in quite a normal way; exacerbations and remissions alternate as previously, while the temperature-values rise and fall or quite rarely also remain stationary. Decrease and increase may possess a very different intensity, and may also be combined in quite a regular way. In yet other cases an uninterrupted, finally enormous increase or decrease begins with the change to a lethal termination.

In the AGONY the temperature is very various. Sometimes the influence of the daily fluctuation is also here still to be recognized: the patient dies without any remarkable changes in the course of temperature, either in the exacerbation or in the remission. But frequently a moderate increase of temperature occurs in those who were previously feverish. At other times a very considerable decrease, from febrile to collapse-temperatures, which contrasts very much with the former course, appears near death, particularly in serious inanition, after severe hæmorrhages, abundant evacuations of fæces, perforations. Finally, the intense pre-mortal temperature-increase, in which the highest values which have yet been observed are attained within a few hours, is in a high degree characteristic. It appears at the close of an intense febrile course, as present particularly in infectious diseases, *e.g.*, typhoid fever, exanthematous typhus; also measles, scarlatina, small-pox, pyæmia; furthermore, in insolation, pneumonia, erysipelas, acute rheumatism, endocarditis; or it forms the termination in diseases of the nerve-centres, as well febrile inflammatory disorders as meningitis and encephalitis; also in affections without any certain tissue-change, especially tetanus, epilepsy, hysteria, which have usually shown a normal or hardly increased temperature until the occurrence of the agony. While with previously intense fever the lethal increase can be accepted as an expression of its highest and therefore most pernicious increase, it appears that, in the last-named affections, it is necessary to believe that a new process has been added, which is frequently indicated by nothing so early and so undoubtedly, as by the enormous increase of temperature.

In the pre-mortal excess of temperature the further increase occasionally ceases at the moment of the cessation of the heart's activity and of respiration; but very frequently a further increase to a very small height, or even to several tenths of a degree, appears for from a few minutes to almost an hour. This post-mortal increase is always terminated by the temperature maintaining a perfectly equal high state, which may exist for several minutes to a quarter of an hour. After that, the temperature falls with varying rapidity, first slowly, then gradually more quickly. In a less characteristic way a post-mortal increase can also occur without a pre-mortal increase.

The highest agony-temperature which has been observed amounted to 44.75° C.; it occurred in a case of spontaneous tetanus. The temperature rose after death for 55 minutes to 45.38° C. Values of 42° C. and more in the agony are quite frequent in infectious and nervous diseases.

Not always does the pre-mortal increase of temperature last to the moment of death ; occasionally it ceases even several minutes before. In this case the decrease may continue after the cessation of the heart's action and of respiration, and increases steadily ; or a short post-mortal increase may first intervene.

CHRONIC DISEASES are characterized by the great changeableness of their course. Normal temperature and fever, as also all fever-types, may alternate in the greatest variety. The separate consecutive days of the disease not rarely possess an extraordinarily variable febrile course: the largest differences between morning and evening, between daily maximum and daily minimum, between the temperature-values of two consecutive days, are possible here. Therefore, the judgment of these diseases, and especially of the effect of antipyretic medicines, is made difficult to a high degree.

Chronic diseases not rarely develop from the acute, and therefore the commencement of the fever may be just as in the latter. At other times they originate gradually ; their beginning is in this case frequently characterized by very inconsiderable but growing rises in the evening temperature for months, which finally also lead to morning increase (*vide supra*). They generally terminate by a very gradual disappearance of the increased temperatures, still much more slowly than by a protracted lysis. Fever-paroxysms, which, more or less intense, interrupt the decrease of the temperature, are of frequent occurrence. The establishment of a perfectly normal temperature is deferred usually by the appearance for a long time of moderate increase of the morning, and particularly also of the evening temperature, which indicates the preceding disorder, and cause an apprehension for a new exacerbation. The fatal termination appears rarely with abnormally increased, usually with moderate febrile height, or with normal and sub-normal temperatures. The latter is sufficiently explained by the very great emaciation of many persons having chronic diseases in the last years of life, produced by a more or less complete inanition. Therefore, post-mortal increase is much rarer than in acute diseases.

The ANATOMICAL CHANGES, which are produced by fever in the solid and fluid parts of the organism, are of very variable kind. They are partly induced by the permanent influence of high temperature, partly dependent upon the febrile waste in the different fluids and tissues of the body. They are most characteristic in cases of febrile marasmus.

The anatomical changes occurring in consequence of the influence of HIGH TEMPERATURE for many days are found most frequently in fatal cases of acute infectious diseases (measles, scarlatina, small-pox, exanthematous typhus, and typhoid fever, puerperal fever, erysipelas, acute articular rheumatism, etc.). They consist especially of more or less extensive albuminous infiltration of many cellular elements, particularly of the glandular cells of the liver, kidneys, also of the spleen, lymphatic glands, of the colorless blood-corpuscles, of the muscular fibres of the trunk, the extremities and particularly of the heart ; occasionally also of simultaneous moderate fatty metamorphosis of the same parts, as also of waxy degeneration of the muscles. The blood in the heart and in the large vessels is nearly always fluid, or not completely coagulated.

Of old, SYDENHAM, BOERHAAVE, SWIETEN, later ROGER, WUNDERLICH and others, but above all LIEBERMEISTER (*D. Klin.*, 1859, No. 40 ; *D. Arch. f. klin.*

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Med., 1866, I., pp. 298 and 592), have called special attention to the regularity and importance of the above-mentioned tissue-changes, especially of the albuminous infiltration, in high fever. According to L., these changes are in many cases the consequence of the increased bodily temperature, and frequently the only cause of death. L. proves this by the constant occurrence of albuminous infiltration in the cited conditions, by pointing to the noxious, even deleterious influence of higher temperatures upon living cellular organs (SCHULTZE, *Das Protoplasma, u. s. w.*, 1863, p. 33 et seq.—KÜHNE, *Arch. f. Anat., Phys., u. s. w.*, 1859; *Unters. üb. d. Protopl., u. s. w.*, 1864), to the favorable influence of cold-water treatment, by the similarity with the conditions after sunstroke or insolation (*vide* p. 59).

Also consult BUHL, *Z. f. rat. Med.*, 1857, VIII., p. 89; 1858, IV., p. 304.—HOFFMANN, *Unters. üb. Abdominal-typh.* 1869.

Against LIEBERMEISTER'S interpretation a number of important objections can be made. First, the parenchymatous infiltration is either entirely absent in some cases of high fever lasting several days, or is only present in a very minute degree. Furthermore, the same infiltration occurs under conditions in which only slight fever or none existed : *e.g.* in some very extensive rapidly fatal burns (*vide* p. 298), in some cases of suffocation, in some cases of poisoning (by sulphuric acid, muriatic acid, phosphorus). In special cases almost always yet other causes of albuminous infiltration enter into consideration : the infectious substance, as in the acute exanthemata, in pyæmia, etc. ; anæmia or hyperæmia, and acute consumption ; the disordered respiration. The colloid degeneration of the muscles is also believed by some to be the consequence of fever ; but this is present under such various circumstances, that its causes must also be considered as unknown.

According to SWIETEN, and later to WEIKART, death in excessive increase of the bodily temperature results from coagulation of the fibrin of the blood at about 43° C. (*Arch. d. Heilk.*, 1863, IV., p. 193). But just in those diseases in which death results most frequently by excessively high temperature, the amount of fibrin in the blood is small ; frequently all blood in the corpse is still liquid, or forms but flabby coagula. In death by sunstroke, etc., also, the blood is usually fluid.

The anatomical changes which appear in consequence of the FEBRILE WASTE are in the main analogous to those of senile and pathic marasmus. They consist of dryness of all tissues, of their simple atrophy and emaciation. In regard to changes in the blood *vide* p. 533. Their immediate cause is probably an actual consumption of bodily ingredients, analogous to that of inanition.

The FUNCTIONAL DISORDERS, which we observe more or less constantly in fever-patients, have their origin mainly in the disordered temperature and most particularly in the increase of the body-heat. They occur in the nervous system, the organs of circulation and respiration, the digestive apparatus, and the secretions.

In respect to the nervous phenomena, general sensation (*gemeingefühl*), and the senses as well as the psychical and motor functions present important changes.

General sensation is almost always disordered in fever. At its commencement there is frequently an increased sensibility, especially in regard to heat-abstracting influences, and actual cold. Notwithstanding warm covering the patient feels chilly and shudders (horripilation), partly in the extremities, partly along the back ; the peripheral parts, as ears, nose, fingers and toes, become cold. In this degree the chilliness may continue for hours and days, or increase rapidly to chills (*vide* p. 610), particularly in severe febrile affections. In the chill the face and extremities, or even the entire skin, including the visible mucous membranes, become cool and bluish, the skin-turgor is diminished, the eyeballs are sunken, respiration is more frequent ; the patient feels oppressed and extremely miserable and uncomfortable, he experiences nausea and occasionally vomits ; he reposes upon his side and bends himself up, as though to decrease the losses of heat by diminishing his bulk ; he throws himself about spasmodically, as though

to increase the production of warmth by muscular activity; he shivers freely, and the lower jaw moves rapidly up and down, even so as to produce chattering of the teeth. In this way the chill may continue for a few minutes or hours, and its intensity may gradually and continuously diminish, or again increase for a short time to its former severity. As a rule, the body-heat during the chill is very considerably increased in the internal parts of the body, and the chill is finally thereby completed, an equalization gradually occurring between the periphery and the internal parts; at the most, short light shudders appear now and then. If a chill has been attained, the period of cold is as a rule followed, as reaction, by a warm stage with feeling of intense heat, strong injection of the skin, especially of the face, turgescent skin, which gradually begins to perspire, and therewith subsidence of the preceding subjective complaints.

The chill is best characterized and strongest in primary pneumonia, intermittent fever, and pyæmia. Occasionally a chill exactly like this occurs without fever, *e.g.*, by passage of a urethral catheter, by impaction of a urinary calculus, etc.
Very conspicuous are the contractions, in chills, of the unstriped muscular fibres situated around the cutaneous glands, whence arises the characteristic appearance of "goose-flesh." The simultaneous cyanotic discoloration is explained by the spasmodic contraction of the unstriped muscle-cells of the cutaneous vessels, from which the arterial afflux is excluded, and the rapidity of the blood-current through the small veins impeded.

Excluding these symptoms of chills, which are especially important and frequent in the beginning of fever, we meet throughout its whole duration numerous other psychical, sensorial, and probably also motorial symptoms. In the slightest degrees of fever no disorder whatever of consciousness exists. There is present an uncertain sense of indisposition, restlessness, excitement, oppression; heaviness and dulness of the head, headache, disinclination to mental occupation; sensibility toward all impressions of the senses; restless sleep with oppressive dreams; painful sense of fatigue of the spine and limbs, a sense of weakness and debility, want of will-energy. In more intense fever appear fainting and dizziness in assuming the erect posture, darkness before the eyes and noises in the ears; moderate apathy, some want of memory, hesitating answers; delirium in a state of half-sleep, occasionally also while waking, and infirm muscular actions. In still higher degrees, consciousness is continuously disordered, though not always to the same degree, and the irritation of the brain presents transitions to symptoms of depression. Restlessness, excitation, continued delirium with fancies, uncertainty in regard to the surroundings, frequent illusions and hallucinations, loud talking and screaming, attempts to leave the bed; light maniacal attacks, *subsultus tendinum;* local twitchings, in small children exceptionally also general convulsions are the symptoms of the irritation of this stage. As severer symptoms of depression are to be regarded quiet delirium, great apathy, stupid expression of the face, muttering delirium, bed-picking, occasional involuntary evacuations of the bowels, frequently sopor without any energetic expression of psychical activity. Higher degrees and longer duration of such phenomena always indicate great danger. In the highest febrile forms continued unconsciousness, sliding down in the bed, and not any or extremely slight reaction upon psychical and sensorial impressions exist.

According to MANASSEIN (*Virch. Arch.*, 1872, LVI., p. 220) the muscular debility occurring regularly in strong fever of short duration, or in slight or intense fever of

longer duration, as well as the frequent pains in the muscles, depend upon diverse changes in them: first upon the frequently existing so-called colloid degeneration (*vide* p. 331); perhaps also upon the more abundant transformation of creatin into creatinin (increase of the latter in the urine: J. LEHMANN, MUNK, GAEHTGENS, HOFMANN); upon the increase[ ]amount of potassa-salts in the urine (SALKOWSKI). Chemical analysis also shows in the muscles themselves a cause acting upon them through the fever: the amount of watery and alcoholic extracts of the muscles is always smaller in feverish animals than in the healthy; the quantity of nitrogen contained in the extracts is larger in the former. NAUNYN (*vide infra*) found in the muscles of dogs on the 3d–5th days of ichor-fever 0.1–0.2 %, in the blood 0.06–0.15 % of urea; similar numbers were obtained in typhoid fever and septicæmia.

If in the above statement the several nervous symptoms are brought into connection with the fever-intensity, it is not to be understood that in each single case and at every time a certain height of temperature is accompanied by the same or similar symptoms of disease. This is not the case; high fever can exist exceptionally almost without any considerable, very slight fever with severe disorder of the nervous system. For this disorder is not only influenced by the height of temperature, but also by many other factors more or less mysterious in their actions,—above all, individuality with its changing excitability at different times and in different persons. At present, therefore, it cannot be determined whether the disorder of the central organs depends upon demonstrable material changes, the less so as more accurate examinations of those who died after severe fever are not recorded. It can only be said, that the anatomical changes causing the lower degrees of nervous disturbances must be such as admit of rapid recovery, as the duration of those symptoms is as a rule short, and in the main limited by the duration of the excessive increase of temperature.

The symptoms in the VASCULAR SYSTEM are very important. Before the knowledge of the results of thermometrical measurements they were especially relied upon in the study of fever.

With the increase of temperature in fever the heart's movements are accelerated, and the heart's pulsation strengthened; also, not rarely, there is present in place of the first sound in the ventricles as well as in the arteries a systolic murmur, or at least an intermediate form between sound and murmur. The larger arteries, as the carotids, are seen to pulsate more strongly. The small arteries of the skin are contracted during a chill, so that it appears paler, and, as the insufficient afflux of arterial blood is accompanied by venous repletion, at the same time becomes of a bluish color. During febrile heat the cutaneous arteries are relaxed, the capillaries better filled, the veins empty, the skin turgescent, red, not livid. This febrile flush is of course most strongly marked in parts having abundant capillaries and a thin epidermis: cheeks, lips, conjunctivæ, therefore appear especially reddened. Occasionally the distribution of the blood is not uniform.

The conditions of the ARTERIAL PULSE during fever has received quite special attention. Best known is the increase in the frequency of the pulse. Formerly the acceleration of the heart's contractions were even accepted as pathognomonic of fever; but this is now, after the new standard which thermometrical observation has produced, no more admissible. But the increased frequency of the pulse is nevertheless that symptom which, next to the increase of the body-heat, is observed most constantly in fever, for they stand in the closest relation with each other.

By counting the pulse-beats of a patient we wish to gain a criterion for judging the influence which the morbid process exerts upon the circulatory apparatus. But, besides the bodily temperature, the following conditions must also be taken into consideration in forming this judgment: constitutional conditions (anæmia; intoxication, *e.g.*, with lead, and infectious matter, *e.g.*, with scarlatina); the condition of the heart itself (inflammation, valvular disease); the degree of resistance in the vascular system (renal

affections, dropsy, pleuritic exudations); the action of those parts of the central nervous system important to the heart's movement. It is therefore not surprising, that a certain height of temperature is by no means accompanied by a given frequency of the heart's pulsations; but just as little are all these various influences able, in a given case, entirely to set aside the influence of temperature.

It can be proven with certainty, as a rule, that in fever *ceteris paribus* the frequency of the pulse is the greater, the higher the bodily temperature rises. A simple statistical compilation of numerous observations of the pulse in fever-patients is sufficient to demonstrate that dependence.

LIEBERMEISTER (*D. Arch. f. klin. Med.*, I., p. 466) has calculated from a considerable number of simultaneous pulse and temperature observations the following values for adults :

Temperature,	37° C.	38° C.	39° C.	40° C.	41° C.	42° C.
Pulse { minimum,	45	44	52	64	66	88
maximum,	124	148	160	158	160	168
average,	78.6	88.1	97.2	105.3	109.6	121.7.

It is thus shown, that, notwithstanding all fluctuations, and notwithstanding the great divergence of the maxima and minima, the arithmetical average of the frequency of the pulse increases equally with the increase of temperature, so that an increase of the latter of 1° C. is accompanied on the average by an increase of the pulse of eight pulsations per minute.

Furthermore the influence of the temperature upon the frequency of the pulse is proved by : the condition of the latter upon artificial increase of the former, the rise and fall of the frequency of the pulse in the foetus of a feverish pregnant woman being in proportion to the mother's temperature ; as also, lastly, by physiological experiment. If a fluid of variable temperature is allowed to circulate through separated hearts, the frequency of the heart's pulsations rises and falls in proportion to the temperature ; near the normal temperature greater irritability of the heart is evident, characterized by a greater increase of the frequency relatively to a smaller increase of the temperature ; by too great an increase of temperature the irritability of the organ is entirely destroyed.

The influence of temperature in disease, however, becomes evident under very variable conditions. With the same height of temperature, furthermore with equality of age, size and sex, of the nourishment and the position of the body, with the same extraneous circumstances generally, we find greatly diverging frequency of the pulse. It is not, therefore, the absolute pulse-frequency which is influenced in a feverish person by the temperature-height, but only, so long as disturbing elements do not arise, its daily movement.

Not less important is the CHARACTER OF THE ARTERIAL PULSE. An experienced observer should distinguish by the finger, besides the frequency of the pulse, also : whether it fills quickly or gradually (*pulsus celer, pulsus tardus*) ; how high the pulse wave is (*p. magnus* and *parvus*) ; how widely the artery is distended (*p. plenus* and *vacuus*) ; in what degree of average tension the artery is (*p. mollis* and *durus*). The fever-pulse of a previously healthy adult is more or less large, full, hard, quick, and probably it gains these properties mainly through the influence of a quicker and stronger contraction of the heart. Characteristic examples of this are presented in acute inflammations, especially pneumonia, less strikingly in infectious diseases. Self-evidently the forms of the pulse of feverish persons vary greatly according to the original constitution of the pulse before the occur-

rence of the fever, as also according to the influence which the disease has until then exerted upon the texture and function of the heart. Even during a febrile condition a small, empty, soft pulse can very well exist transiently or continuously, but only under the influence of particular circumstances, which more or less paralyse that of the fever.

Much more clearly than by palpation with the practised hand, though this, notwithstanding, cannot be dispensed with, is the change of the pulse, produced in consequence of the fever, represented in its delineation by means of the SPHYGMOGRAPH. The accurate representation, only very superficially possible without an instrument, of the wavy motions of the arterial tube, is one of the great advantages of sphygmography.

According to O. J. B. WOLFF (*Charakteristik des Arterienpulses*, 1865), who employed MAREY's sphygmograph, three parts can be distinguished in every drawing of one pulsation of the radial artery of a healthy adult: the ascending curve, the apex and the descending curve. The first, the ascension-line, is the steeper, the more quickly the expansion of the vessel is completed: it always only deviates very slightly from the vertical line (*i.e.*, the circle, which the lever of the apparatus describes upon the blackened paper). It approximates the latter the closer, the less the elasticity of the vessel's walls and the more energetic the quickness of the heart's contractions (as in the *pulsus celer*). The apex of the curve is in a correct drawing always only a point, the point of an acute angle. The descending curve, descension-line, possesses normally two main waves; occasionally a third one is added, accordingly as the tension of the aorta diminishes quickly or slowly. In a small pulse the first of the two main descension waves appears to be the larger. If three waves exist, the first, commonly the smaller wave, is to be considered as divided into two. If, as is usually the case, the last wave (large ascension wave of WOLFF) alone is well marked, the pulse is also distinctly perceived by the finger as consisting of two waves (double beat, dicrotie); in anæmic convalescents the three waves are probably also detectable by attentive observation. In a careful drawing and sufficiently large pulse several other small waxes are found on the descension line. Its wavy appearance arises from the vibrations of the arterial wall made varyingly tense by the heart's systole, and is modified by the unequal elasticity of the wall, as well as, especially in the larger arteries, through the influence of the return current of the blood toward the heart during the heart's diastole, whereby the intravascular pressure is quickly diminished.

The normal pulse-curve is somewhat different according to age. The pulse of aged persons is also tricrotic, *i.e.*, it has besides the main ascension-wave also two larger (secondary) waves upon the descension line. It is especially characterized by the second impulse of each pulsation (first secondary wave, in the above described pulse of the adult small) possessing a very considerable size and duration; besides that, the apex angle is very acute (considerable celerity). In the child's pulse also the first secondary wave is larger than in the adults, on account of the shorter distance of the heart from the artery examined.

In increased temperature the radial pulse-curve of a healthy adult changes in the following way. If the axillary temperature increase but by several tenths of a degree, at the most to 38.5 C., the pulse-curve becomes incompletely dicrotic, subdicrotic; *i.e.*, the incision between the first and second descension waves becomes larger, and thereby also the height of the second wave (the so-called great ascension wave) more considerable. The first descension wave is never divided into two portions. If the temperature rise to 39° C. and above, the pulse becomes constantly more dicrotic; it is completely dicrotic at 39.5° to 40.5 C. The dicrotic curve is characterized by the first secondary wave having become still smaller, and the incision between it and the second wave extending still further down, to the base of the curve, *i e.*, to the point whence the ascension line began. In this way the second secondary wave has enlarged very much, and also appears later as in normal conditions. It is distinctly felt by palpation, every contraction of the heart being followed by a double pulsation. Dicrotism is best marked in a soft pulse, *e.g.*, in typhoid fever, although it is more or less observable in all severe acute diseases. In a further increase of temperature the perfect dicrotism is surpassed, *i.e.*, the large incision just mentioned between the first and second secondary waves becomes still deeper, so that its point comes to be placed beneath the base of the curve. At the same time the first secondary wave is reduced to a minimum: it appears only as a slight unevenness of the beginning of the descension-line. Usually the pulse has also become considerably smaller; especially

is this seen in the second secondary wave, which appears so well in dicrotism. This type is called superdicrotic; it is present in a temperature of 41° C. and more. Finally the highest temperatures are accompanied by a pulse, in whose curve (small on account of the exceedingly rapid contractions) the second large secondary wave (large ascension) also has been reduced to a slight inequality or has entirely disappeared. The descension line appears therefore as a line sinking quickly and considerably beneath the base of the curve, and thereupon rising slowly a little . toward the straight-running ascension division of the next pulse-wave. This is the monocrotic type. Between the several curve-types all possible intermediate and transitional stages exist in reality.

If the temperature fall, in the healthy, to the lowest normal values, trierotism is more clearly marked than in the average normal values. In the main the same condition of the pulse-curve appears co-existing with collapse-temperatures in the sick, with healthy nervous systems. Extraordinarily low temperature-values but very rarely occur in such; they have been observed much more frequently in psychical disorders, therefore with the more or less well marked *pulsus tardus* peculiar to them (in contrast to the somewhat quick pulse of the healthy). The extremest degrees of slowness of the pulse (*p. monocroto-tardus*, WOLFF) are accordingly present in psychoses with extremely low temperature. For further information in regard to this, see WOLFF, l. c.; and *Allg. Zschr. f. Psych.*, XXIV., pp. 409 et 586; XXV., pp. 305 et 730.

All facts tend to prove that the manner of the vibration of the arterial wall is influenced by diverse factors, as blood-pressure, size, repletion, frequency, hardness, tension of the pulse, and that the exceedingly various conditions of the pulse cannot be explained by one single cause. At any rate, the conditions of excitability of the centres of the vaso-motor nerves concur very considerably in their origin; but the closer connection is not understood. Most important, for the study of fever, of the facts gained through sphygmography, is the demonstration of a moderate dicrotism of the pulse in healthy persons with normal temperature, which becomes with febrile increase of the body-heat through the described changes in the descension line of the pulse-curve so distinct and characteristic, that even the finger is able to detect it readily.

CHANGES IN RESPIRATION occur in all diseases attended by fever, not only in those of the respiratory organs.

Above all, the number of respirations is increased, occasionally quite considerably. It is under otherwise similar circumstances, different according to the intensity of the fever and to the age, as also to the sensitiveness and hardiness of the persons examined. With average height of temperature a robust adult breathes 20–30, a child 30–40 times a minute; with high temperatures the former 30–40, the latter to 60 times; younger children breathe still more frequently. Robust individuals with extensive thorax and little nervous excitability present even in high fever not rarely only an inconsiderable increase in the respiratory frequency, while in feeble persons with excitable character of the fever, respiration may become exceedingly frequent and dyspnœaic, without the presence of pulmonary or cardiac affections.

Already, on account of the circumstance that increased warmth increases the excitability of the nerves and of the functions generally, it is probable that it is capable of producing *per se* an increased frequency of respiration. Furthermore, the intimate relations between the former and the latter, meaning that the change of respiration in fever is the consequence of increased body-heat, are proven by those cases of disease in which, without any affection of the respiratory organs, it rises and falls with the daily fluctuations of the latter, as well as by those in which with a decided affection of those organs, *e.g.*, in croupous pneumonia, it falls from considerably increased numbers to the normal with the critical defervescence, without the exudation having changed in any way. The same power of decreasing the respirations is possessed by all means of abstracting

heat, of reducing sufficiently the febrile increase of body-heat; and that in proportion to the degree of decrease of the temperature. In the same way, artificial increase of the body-heat produces a simultaneous considerable increase of the respiratory frequency; with the cessation of the temperature-increasing influence the number of respirations rapidly falls to the normal.

If ACKERMANN (*D. Arch. f. kl. Med.*, II., p. 360) held an artificially strongly heated and extremely rapidly breathing dog in cold water, the respiratory orifices alone remaining out, or if he cooled him rapidly by some other means, the normal frequency of breathing was just as rapidly (in several minutes) re-established. The same happened if he injected cold defibrinated blood in not too minute quantity rapidly toward the lungs into the jugular veins; but if he employed for this warm blood, it did not occur. In high temperature of the animal artificial respiration has no great influence upon the frequency of its independent respirations, not even when in consequence of the inflation of air the blood in the veins shows a light red color; while through artificial respiration in low temperatures of the animal the breathing is reduced in frequency, and is even brought to a stand in the usual temperature.

Even if it appears, in accordance with all the facts, that the increase of respiration in fever is caused by rise of the body-heat—and it is not probable that there are any other factors in fever—we do not mean to assert that there are not accessory elements having a certain influence. In some diseases such elements are easily recognized: such, for instance, are the hindrances to respiration which interfere with the exchanges between the blood and atmospheric air, such as occur in diseases of the respiratory passages; and also in inflammatory changes, and particularly when a pain occurs at the height of inspiration.

The type of respiration is not altered by the occurrence of fever, as such; in the beginning of the disease, in well-nourished persons, the depth of inspirations is often increased. Usually, with the appearance and progress of febrile emaciation and exhaustion, they become more superficial owing to weakness of the respiratory muscles, and thereby there are not rarely produced hypostatic affections of the bronchi and lungs.

RIEGEL (*Athembewegungen*, Würtzb., 1873) noticed in observations made upon fever-patients by means of the stethograph, very often great irregularity in the individual respirations; deep ones succeeding in a wholly irregular manner to superficial ones. There occurred, repeatedly, short or long pauses in the breathing, as well as disorder in the relative duration of inspiration and expiration. He, consequently, denies the existence of a constant change in the mechanism of breathing in fever.

The observations of LEYDEN (*D. Arch. f. kl. Med.*, VII., p. 536), made by another method, in which by means of resistance of the apparatus the volumes of air expired during a quarter of an hour was directly measured in febrile and in non-febrile states, showed a notable increase in amount of air breathed in fever; in the proportion of $1\frac{2}{4}$–$1\frac{1}{2}$: 1. The mean measurement obtained from all the observations corresponded with that of each series of observations.

In the last few years the EXCRETION OF CARBONIC ACID from the lungs in fever has been studied with especial care, because it was thought that by this a measure for the estimation of the amount of tissue-metamorphosis might be obtained.

The following results have been obtained by physiological observation, and they bear a certain relation to the events in fever (consult WUNDT, *Physiologie*, 3 Aufl., 1873). The stay of an animal in air of a temperature which increases his body-heat, increases, during the greater frequency of the respirations, the excretion of carbonic acid, and the absorption of oxygen. On the contrary, in a temperature which diminishes the body-heat, the amount of CO_2 expired is lessened; but in this case the

deerease in the absorbed O is not proportional, but the oxygen, at the first dimin-
ished, is notably increased after prolonged action of the low temperature. Slight
variations of temperature, such as do not affect the body-heat, appear to have no
effect upon respiratory processes. As a rule, the amount of CO_2 is increased in more
frequent respiratory movements. With deeper inspirations, the absolute quantity of
CO_2 expired is increased, while the relative proportion of CO_2 in the expired air
is diminished; because a larger volume of air can diffuse more carbonic acid than
a smaller, and at the same time a larger volume of air becomes more slowly saturated
with the gas. In general, the amount of expired CO_2 increases with the amount of
carbon in the food. Among the substances which contain much carbon, the carbo-
hydrates which have more O in their composition cause the exertion of much more
CO_2 than do the fats and albuminates which contain less O. This is probably owing
to the fact that the O contained in carbo-hydrates requires their H for the forma-
tion of water, so that the whole of the inspired O can be used for the combustion
of the C into CO_2; while the albuminates and fats containing less O are split up into
products of oxidation which are poorer in O than CO_2, and pass into other exertions.
The taking of food usually produces an increase in the exertion of CO_2, beginning very
soon after a meal, reaches its maximum in 2–3 hours, and then decreases. A decided
decrease in the exchange of gases results from the withholding of food, and if this
be persevered in so as to cause death by starvation, the exertion of CO_2 continues to
diminish with great rapidity, especially toward the close of life. This excretion is
so much increased by muscular exertion, that it may be rendered even three times
as great. Correspondingly with the greater exchange of gases, the respirations are
increased in depth and frequency.

LEYDEN (l. e., p. 555) found in fever, together with decrease of the percentage of
CO_2 in the expired air (on the average in the relation of 3 in the feverish to $3\frac{1}{2}$ in the
non-febrile state), because of the greater quantity of the air, an increase of CO_2 in
the proportion of nearly $1\frac{1}{2}$: 1. This result is obtained from a large number of
observations on patients affected with different febrile diseases, and is in general
indisputable, although the method is not faultless, and the individual experiments do
not appear absolutely demonstrative.

LIEBERMEISTER (*Ibid.*, VIII., p. 159) found, in attacks of intermittent fever, that
the production of CO_2 was greater during the apyrexia, although the difference was
not striking. He was unable to determine a constant relation between degrees of
temperature and the exertion of CO_2. SHRÖDER also (*Ibid.*, VI., p. 385) observed an
increase of CO_2 in fever, as much as 57% according to SENATOR'S calculation.

SENATOR estimates that the increased exertion of CO_2 amounts to 57% of the
normal at the farthest, and as a mean quantity 37%. This exertion must, however,
by no means be taken as equivalent to increased production of CO_2, for in fever cir-
cumstances are very favorable to exertion (increased ventilation of the lungs by
accelerated breathing, increased diffusion, etc.).

A CRITICAL INCREASE of expired CO_2, comparable to that of urea, has
not yet been observed.

According to SENATOR (*Fieberhft. Process.*, Berlin, 1873), this is to be explained
by the facts that in man during fever the conditions are more favorable for the
separation of CO_2 than for the exertion of urea, because an accumulation of sub-
stances rich in C and devoid of N does not take place.

Lastly, the evaporation of water from the lungs is increased in fever,
inasmuch as the volume of expired air is larger and warmer than that of
the non-febrile state.

THE PHENOMENA IN THE DIGESTIVE APPARATUS in febrile diseases, which
are chiefly interesting to the practitioner, have been as yet but little
studied.

The function of digestion is so much disordered that, usually, the appe-
tite is diminished or wholly lost, the thirst is increased, constipation is
present. At the commencement of fever, chiefly in children and in dis-
eases which are ushered in by a chill, and also shortly after preceding
ingestion of abundant food difficult of digestion, severe vomiting, occurring

once or more, is present, and tends to divert the physician's attention from the disease itself. This easily destroys the appetite entirely, whereas, in children, moderate vomiting at the beginning of febrile diseases often exerts a favorable influence, and under certain circumstances is to be encouraged. Occasionally in the first few days even of a quite severe fever the appetite is unchanged, as, for example, in the relapses of typhoid fever it may even be excellent; though in such cases vomiting is easily induced, and complete anorexia ensues. Occasionally the appetite is tolerably well preserved during the whole duration of the affection, and there may be longing for substantial articles of food, the gratification of which a cautious physician will delay and restrict. For it is the rule to see, after the ingestion of large quantities of food, perhaps against the patient's inclination, symptoms of dyspepsia or even of gastric catarrh. All facts go to show that fever exerts considerable influence in diminishing and destroying desire for food, and in disordering digestion. The disorder of digestion is in a measure intelligible, if we recall that all secretions, and most probably all of the digestive fluids, are diminished in quantity and quality. The diminution of appetite cannot be satisfactorily explained, as long as we are not better acquainted with the physiological mechanism of hunger in the healthy state: we must be contented to designate the dislike for food as an instinctive feeling, which is likewise present in many other disorders of gastric digestion. After the cessation of fever, or toward the close of the febrile period, the appetite and digestive power return, if there exist no gastric or intestinal disease.

The question, so all-important for rational therapeutics, whether the secretion of digestive fluids is diminished and altered, has hitherto been studied in a very insufficient manner. Undoubtedly, the only irreproachable though exceedingly difficult method to determine the question of the activity of the digestive organs in febrile conditions, consists in careful weighing of the nitrogenous and non-nitrogenous foods given to the fever-patient, and in a not less careful and exact analysis of the fæces of the patient.

Hitherto various opinions, untenable in many respects, have been held on this question, because the erroneous results of old experiments and observations (BEAUMONT) upon gastric digestion were applied without reserve to digestion in general. Besides, absolutely contradictory observations were made: while by means of gastric fistulæ in man and animals (SCHIFF and BEAUMONT) it was noted that the activity of the stomach was either diminished or abolished in fever, the more recent investigations of PAVY, HOPPE-SEYLER, and others, by means of infusions of the gastric mucous membrane of men who had died of fever, showed preservation of the digestive power. The causes of these contradictory results lie in the methods employed. MANASSEIN (Virchow's Archiv, LV., p. 413) procured "natural gastric juice" by means of sponges swallowed and withdrawn, and made "artificial gastric juice" from the well-washed gastric mucous membrane of the same animal with the addition of dilute hydrochloric acid. In the course of his investigations, he found that the natural feebly acid gastric juice of a feverish animal (with septicæmia) had much less digestive power than the more acid secretion from a healthy animal. The assumption that in the above-named fever the pepsin is thrown out without an accompanying proportionate amount of acid, is in agreement with the opinion that the two substances are produced in different parts of the stomach; a view which is supported by many other facts. In the "artificial gastric juice" of feverish animals he found that fibrin was better, and albumen not as well digested as in artificial gastric juice of the healthy animal. In this connection it should be noted, that the gastric infusion from the feverish animal was slightly though constantly more acid than that from the healthy animal; although the latter had previously furnished a large amount of "natural gastric juice." According to M. the administration of acids improves the digestion of animals.

Of the other digestive fluids only the PAROTID SECRETION has been carefully studied.

Mosler often tried to test this in febrile diseases, obtaining it by means of a canula inserted in Steno's duct. This was, nearly always, in small quantities, and, especially when distinct digestive disorder was present, of acid reaction, though it was not possible to determine the free acid. He supposes that owing to the increased tissue-metamorphosis in fever the epithelium of the gland-ducts is cast off more rapidly, and that the acid reaction is produced by chemical changes within the cells. In the normal state, according to ORDENSTEIN, the saliva from the parotid gland is constantly alkaline, and only in the fasting state does it regularly show an acid or neutral reaction. In other cases M. was unable, although using all means to excite the secretion (irritation of the buccal mucous membrane, masticatory movements), to obtain a single drop of liquid. It would seem as if the secretions were often wholly abolished, as it would seem right to infer from the simultaneous dryness of the mouth and pharynx. The introduction of a canula is of practical importance, according to M., for the removal of obstruction in Steno's duct and of accumulated secretion, an important cause of parotid inflammation in severe febrile diseases, especially typhoid fever.

Seldom does fever exist without an INCREASE OF THIRST; and this may be so great that ordinary drinks (cold water, lemonade) afford relief only for a few minutes. This state is not caused by febrile desiccation of the body. It is partly dependent upon the severity of the buccal and pharyngeal catarrh, which accompanies every intense fever, as well as upon changes in the gastric mucous membrane. Dryness of the mucous membrane of the mouth, particularly that of the tongue, and its consequences, are usually relieved by early and carefully done cold-water treatment of the fever. The direct dependence of the dryness of the buccal mucous membrane upon the height of the temperature is demonstrated by the effect of severe collapse, as, for instance, upon the occurrence of intestinal hæmorrhage in typhoid fever; in which case the tongue becomes moist when the temperature falls, in spite of depletion of the vascular system, and only becomes dry again when the fever again increases.

CONSTIPATION is the rule in fever, except when increased mucous secretion is produced by catarrhal inflammation of the intestines. The constipation is most probably the result of diminished ingestion of food, and consequent weaker peristaltic action of the bowels; though, probably, a primary lessened secretion of intestinal fluids may also act as a cause.

EVAPORATION FROM THE SURFACE OF THE SKIN is changed in every case of fever, and without doubt this condition is one of the important means of moderating the febrile state. Evaporation takes place either insensibly (insensible perspiration), or appears in the form of sweat. Both forms, insensible evaporation and sweating, are identical in kind, though different in degree and appearance; sweat being the expression of the greatest amount of cutaneous secretion, in the shape of visible drops.

Among the three modes of exhalation of water from the body, that by the skin is the most variable, even subject to incessant fluctuations, while the pulmonary exhalation is less, and the renal excretion least subject to disturbance by external and internal conditions. The relations of cutaneous exhalation to the body-heat and to the frequency of the pulse are very intimate. On the average it rises and falls in the same ratio as the two last, if no special factors, such as local applications of cold, destroy the uniformity of the conditions; it increases in very various degrees with the progressive elevation of the average normal temperature. In fever, on the contrary, the amount of perspiration depends less upon the degree of temperature than upon certain peculiarities of the disease: we consequently often observe sometimes a dry, sometimes a wet skin, with high body-temperature. For instance, the skin is dry in the chill-period of fever, in the majority of cases

of typhoid fever, of pneumonia, scarlet fever, the eruptive fevers in general; it is found covered with sweat, frequently in equally considerable elevations of temperature, in acute rheumatism, puerperal fever, miliary tuberculosis, etc. The most copious febrile sweats are observed in the stage of defervescence, more especially if this take the form of crisis, though not rarely also with the morning falling of temperature of lysis, as, for example, in typhoid fever, and in hectic fever. The best known is the abundant secretion of perspiration in the sweating stage of malarial intermittent fever, and in the crisis of pneumonia. In spite of these facts, it cannot be assumed that there exists any immediate relation between the secretion of sweat and febrile heat. The fall of temperature of crisis is by no means the consequence of the critical sweat, since, as a rule, the temperature begins to diminish and continues to do so for a while before the secretion appears; and, besides, the amount of heat which is taken from the body by the evaporating water is not large enough to account for such a view. At the most, only a moderate influence on the lowering of temperature can be attributed to it. And, on the other hand, an abundant sweat is as little the result of a great lowering of the temperature as dryness of the skin is the result of a highly febrile condition. It is presumable that the amount of cutaneous exhalation essentially depends upon certain changes and processes in the nervous system which are in close relation to animal heat, just as under physiological circumstances; partly upon the presence or absence of certain chemical products of metamorphosis.

While many (WEYRICH, *Unmerkl. Wasserverd.*, 1862) do not think it necessary to assume the existence of a secretory apparatus other than the general surface of the body to account both for the sweat and for insensible perspiration, it is not probable, in LEYDEN'S opinion (*D. Arch. f. klin. Med.*, V., p. 366), that the sweat is only an increase of the perspiration through the walls of bloodvessels. Much more probably it is to be considered as a true secretion, influenced by other factors than the mere afflux of blood. In the heat of fever, while the vessels of the skin are enlarged and filled with blood, sweating is not observed. At any rate, the occurrence of an important increase of cutaneous secretion cannot be assumed in fever.

NEUMANN (*Inaug. Diss.*, Dorpat, 1873) finds,—in opposition to FREY (*Dorpat. med. Zeitschr.*, 1873, Bd. III., p. 233), who holds that an increase of insensible perspiration in fever is very possible but not necessary, and who does not see any parallelism between the height of the temperature and perspiration,—after experimenting on dogs in whom fever had been induced by the injection of putrid substances, that there constantly appeared an increase of insensible perspiration with an increase of temperature, and he claims that a parallelism does exist. PUDZINOWITSCH (*Med. Centrbl.*, 1871, No. 14) came to dissimilar conclusions.

Upon the question of the CHEMICAL COMPOSITION of febrile sweat in particular, investigations have as yet given no results worth naming. It is not yet certainly established that the sweat always contains UREA (J. RANKE, *versus* FAVRE, FUNKE, L. MEYER, H. MEISSNER). Even if this statement should be verified, the amount of the substance remains wholly unknown. It is presumable that considerable amounts of urea can leave the body in this way; at least it has been repeatedly observed that on days in which copious sweats occurred the amount of urea excreted by the urine was much reduced from the usual quantity, and it has been surmised that the balance had been carried away with the perspiration. Occasionally, also, the surface of the body has been seen covered with a crust consisting of urea, after the evaporation of profuse sweats.

With regard to the excretion of CARBONIC ACID through the skin, it is known that its quantity is not at all comparable to that excreted by the lungs.

AUBERT and LANGE (*Arch. f. d. ges. Phys.*, 1872, VI., p. 549) calculated from their experiments that its amount in twenty-fours reaches a maximum of 6.3 grm., a mini-

mum of 2.3 grm., and a mean of 3.87 grm.,—to be raised to 4 grm. if the head be included in the estimation. The temperature of the external air exerts an undoubted and very great influence upon this exhalation: the higher the temperature the more CO_2 is separated. The following table exhibits the daily amounts of exhalation in one experiment:

In air at 29.6° C. the amount of CO_2 was 2.9 grm.
"	30.0° C.	"	"	3.24	"
"	31.1° C.	"	"	3.78	"
"	32.0 C.	"	"	4.7	"
"	33.0° C.	"	"	6.3	"

And the observer was as comfortable while naked during the experiment in air at 30° C. as when clothed in air at 19° C., while 31° C. and 32° C. proved disagreeable, though inducing sweating. The cause of this increased exhalation in higher temperatures lies in the distention of the capillaries of the skin and increased flow of blood through them. REINHARD (*Zeitschr. f. Biologie*, 1869, V., p. 37) estimates the amount of CO_2 exhaled from the whole skin, upon the basis of the quantity determined to escape from one arm, at a mean of only 2.23 grm. SCHARLING (*Journal f. prakt. Chem.*, XXXVI., p. 455 of year 1845) and RÖHRIG (*Deutsche Klinik*, 1872, p. 209) obtained much larger quantities; the former about 32 grm., the latter 14–19.5 grm. *per diem*.

Better investigations have been made upon the subject of the COLLECTIVE INSENSIBLE LOSSES through the skin and lungs. Compare what is said further on about the body-weight. In general the increase in the losses is permanent.

According to SENATOR (*Fieberhft. Process.*, 1873, p 127), the loss of water constitutes a somewhat larger part of the total loss, although the proportion of carbonic acid is very important. The following are the most reliable figures on the subject: whereas the total loss increases (in fever) by 43 per cent. (LEYDEN), the CO_2, under favorable circumstances, increases by 37 per cent. at the farthest.

The URINE, in persons who were previously healthy and strong, is often secreted in smaller quantities at the beginning of an attack of fever; it may be reduced to 800 C. cent. (one-half the normal) and less. Its amount is seldom quite normal, even more seldom actually increased: both of these states occur with some degree of frequency for a while at the acme of a febrile state, although the rule is that the urine is diminished in this period also; this exception to the rule is observed only in febrile attacks of short duration, as, for example, in ephemeral fever, and in paroxysms of intermittent fever. In general it may be stated that constant diminution of the daily amount of urine indicates that the disease is increasing in intensity, while its steady increase has a contrary meaning. In other respects, the relation of the amount of urine to the period of the fever is very variable, and a general statement respecting this cannot as well be made as in regard to the amount at the height of the fever. Exact analyses of the urine have shown that the reduction in the amount of urine depends upon diminished excretion of water by the kidneys.

What is the final cause of this lessened excretion, whether it is diminution of the blood-pressure, a nervous influence, etc., is not certainly known. The marked increase in evaporation from the skin which accompanies increased body-heat, undoubtedly exerts a considerable influence, and it is presumable that a larger amount of perspiration cannot co-exist with increased renal secretion, and that in a contrary way the extreme renal activity determined by drinking too much, can be reduced. In some few diseases with copious exudation, pleurisy for example, the quantity of urine is somewhat reduced.

According to SENATOR (*Fieberhft. Proc.*, 1873, p. 124), the amount of urine passed

during fever rises and falls in general according to the amount of liquid taken, although in fever a smaller part of the ingested water passes out of the kidneys than in non-febrile states. This is an important difference between the febrile diseases of man and the purulent fever artificially set up in the dog. Exceptions are caused by individual peculiarity, by special features of the disease, by morbid states of the skin and lungs, etc.

NAUNYN (*Arch. f. Anat. Phys.*, *n. s. w.*, 1870, p. 175) found in his experiments upon dogs in whom he had produced fever, and who drank normally, the quantity of watery excretion by the kidneys diminished even more regularly than is the case in feverish men. In the period of "latent fever" (*vide infra*), before the rise of temperature, the quantity of urine was lessened, not on account of simultaneous increase in the exhalation of water by the skin and lungs, but exact weighing showed the cause to be retention (of unknown causation) of water in the body. In a few cases this retention of water lasted some time longer than the period of latent fever, being then succeeded by a copious normal secretion, and consequently increase of the urine. This increase takes place about the time of the greatest height of fever, and is never so considerable as to justify the inference that there is a marked increase in the total amount of urine during the whole course of the fever. SENATOR (*Virch. Archiv*, XLV., p. 395) came to similar conclusions. He explains the phenomenon (increase of urine at one period) by the separation of more urea, a substance which facilitates the transudation of the watery part of the urine.

The COLOR of fever-urine is decidedly darker, yellowish-red to red, without containing blood or biliary pigment; the color is the more marked the less urine there is. It is reckoned that there is a twenty-fold increase of urinary pigment in fever. It is probable that this dark color of the urine of fever-patients is due to the destruction of red blood-corpuscles, whose coloring matter has not been completely oxidized previous to excretion.

NAUNYN (*Arch. f. Anat.*, etc., 1868, 4 Hft.) has shown that if a large amount of blood-pigment is at once set free in the blood, a part of it may pass out unchanged through the kidneys. That this seldom occurs in fever, is owing to the fact that the destruction of red globules takes place gradually and in all parts of the circulatory apparatus.

According to JAFFE (*Virch. Arch.*, XLVII., p. 405), the urine of man constantly contains a red pigment, which he calls urobilin, and which is characterized by a peculiar spectral absorption-band, and in its solution a strong green fluorescence may be produced. It is derived from the bile, of which it is a constant constituent, though it is uncertain whether it is related to the other biliary pigments. Urobilin is present in much larger quantities than normal in all febrile conditions, especially in those which are accompanied by the secretion of scanty, concentrated, and dark urine.

Various opinions are held upon the question of the amount of FREE ACID in the urine of fever. J. VOGEL almost never found it increased, as a rule it was diminished; UNRUH, on the contrary, always observed an increase of its absolute quantity, at least at the acme of acute febrile diseases.

In spite of diminution of the salts of urine in consequence of the taking of less solid food, the SPECIFIC GRAVITY of the urine of fever is, as a rule, increased, usually to more than 1020, chiefly by increase of urea.

It is now firmly established, by numerous recent investigations, that in fever the NITROGENOUS CONSTITUENTS of the urine are excreted in GREATER QUANTITY, at least in comparison with the amount separated in health under similar conditions of feeding; and it is very probable that this increased excretion, which is more or less great according to circumstances, goes hand in hand with the fever-heat. This is now tolerably certain with respect to UREA.

The difference in the excretion of urea, in and out of the febrile period, appears most distinctly in those diseases which last only a short time, and in which a high temperature is quickly followed by a fall to the normal. Thus, particularly in inter-

mittent fever, in which the febrile excretion of urea was first studied by TRAUBE and JOCHMANN, afterward by H. RANKE, UHLE, and others. However, some contradictory results have been obtained, according to which the greatest amount of urea is separated on the day when fever is absent, as advanced by GRIESINGER and HAMMOND. SCHULTZEN at last showed that nearly always the increase of urea was not marked on the day of fever, or on that of apyrexia, and that the opposite conclusion depended more or less upon accidental circumstances. Contrarily, SIDNEY RINGER had already, by means of observations upon the temperature and urine every quarter of an hour, demonstrated anew the most important facts bearing upon this question : showing that the excretion of urea becomes greater even before the period of chill, that it reaches it maximum in that period, begins to decrease in the period of heat, and falls rapidly in the sweating stage. If, as HUPPERT has done (*Archiv der Heilk.*, VII., p. 43), we take the hourly mean of his (RINGER'S) analyses of urine in the various stages, dividing the period preceding the chill into two parts according to its length, we obtain the following :

	Amount of urine, C. cent.	Urea, grm.	Na Cl. grm.
Before the chill	41	0.969	0.073
	60	1.224	0.226
Period of chill	65	1.545	0.290
" heat	60	1.339	0.167
" sweat	50	0.587	0.083

The increase of urea in the chill-period, which may reach a quantity triple of that excreted before, can, according to H., be dependent neither upon food nor drink, but is undoubtedly in close relation to the elevation of body-heat. It is, furthermore, interesting that the amounts of urine and chloride of sodium rise and fall with the quantity of urea, a phenomenon already observed.

UNRUH (*Virch. Archiv*, XLVIII., p. 268) noted, in numerous observations, that, exclusive of the few cases in which on account of peculiar conditions the amount of urea is not increased, the amount of increase is variable in severe fever, and may oscillate between 1.06 and 3.07 times the normal quantity. The average amount obtained by him was 30.576 grm., or 1.7 times the normal quantity in the fasting state.

According to HUPPERT (l. c., p. 37), who gives a very careful collection of numerous old and recent observations, the estimates of excretion of urea in febrile states (medical and surgical cases) may be summed up as indicating that more of this substance is produced than in the healthy state, in spite of the impaired nutrition in fever, and that the amount of urea separated may be taken as an index of the height of the fever. The more carefully the temperature is taken the more the correspondence pointed out above between it and the amount of urea produced is made apparent. The correctness of this last statement has been called in question, while no important objection has been urged against the former. UNRUH (*Virch. Archiv*, XLVIII., p. 273) raises the objection that even with (hardly practicable) constant measurement of the temperature, supposing that this exhibits fluctuations, it can never be exactly determined what is the relation between the varying amounts of urea contained in urine voided from time to time and the varying degrees of body-heat. Besides, it must be remembered that with the above method the errors produced by the taking of food and drink are rendered more glaring: in the period of remission the amount of urine is diminished because of less thirst, and in the period of exacerbation it is increased because of the opposite state. U. consequently thinks that it would be better, instead of making numerous measurements in one day on one individual and comparing the various stages of the fever, to estimate the relation between the urea excretion and the height of temperature with reference to the relation, in other individuals, between nutrition and production of urea.

If it be correct that the amount of urea excreted corresponds to the degree of temperature, then this excretion must be greater in severe continued fever than in a more moderate one, and falls of temperature must be accompanied by simultaneous and corresponding diminutions in the amount of urea. These deductions are not always verified by observation. In some cases an impaired state of nutrition before the fever will suffice to keep the excretion of urea down to a minimum, even during high fever.

Again, this excretion may be larger (with abundant sweating) in mild fever than in severe and continued fever. Furthermore, there is observed, especially at the beginning of the fever, a remarkably small excretion of urea in proportion to the height of temperature, while on the following days, with the same temperature, the urea may reach a remarkable amount. The opposite may also be met with, though rarely.

SIDNEY, RINGER (*vide* HUPPERT. *Arch. d. Heilk.*, p. 44 et seq.) has discovered that in intermittent fever the increased excretion of urea may appear even before the period of chill, in advance of the rise of temperature; while in the febrile attacks of a phthisical person, on the contrary, the urea first increased with the rise of body-heat. A pre-febrile increase of urea has repeatedly been observed just before the relapse of relapsing fever.

Lastly, the amount of urea in the period of cessation of fever is often greater than in the time of greatest fever; and in diseases which end critically there may be, with a perfectly normal temperature, an epicritical excretion of this substance, often greater in amount than what was separated during the febrile period, but never exceeding the normal. Various opinions have been expressed as to the cause of this excessive epicritic excretion of urea, which may continue two or three days. A part of the urea thus separated may very well have been produced during the period of fever.

HUPPERT (*Arch. d. Heilk.*, X., p. 506), in connection with an attempt to solve this question in two cases of relapsing fever in which increased urea-excretion showed itself the day after the short elevation of temperature, expresses himself as follows: "If it can be assumed that during the fever 'stabile organ-albumen' is changed in such a way that it behaves just like 'movable provision-albumen' ('circulation-albumen' of VOIT) toward the disordered functions of the organism, it follows from the various observations that the nitrogenous products of decomposition of this 'provision-albumen' will not be excreted on the day when the fever occurs. Since, according to our present knowledge of the time which the nitrogenous ultimate products of albuminous substances remain in the body, it is not permissible to assume that they are carried away at so late a period in the excretions, we may conclude that during the fever either only the transformation of organ-albumen into provision-albumen is completed, or that during the fever the organ-albumen becomes split up into a simpler non-nitrogenous product (whence the assumption that it is burnt), and into a yet complicated nitrogenous residue which need not be decomposed into other products during the prevalence of the great body-heat, but is so split up for the first time in the next succeeding period. I am more inclined to hold the latter opinion than the former, because the diminution of urea-excretion took place more slowly in E. (patient's initial), who was insufficiently nourished, than in H., who was well nourished. Aside from the facts obtained directly by observation, that increase of urea-excretion may follow the lowering of the temperature and need not take place simultaneously with it, it may, furthermore, be inferred that in rapidly repeated (daily) paroxysms of fever, the additional amount of nitrogen thrown out does not necessarily correspond to the periods of high temperature. In repeated febrile attacks there may occur accumulation of nitrogenous substances."

RIESENFELD (*Virchow's Arch.*, XLVII., p. 130) rejects the idea that the retardation of the excretion of urea can be essentially dependent upon the taking of food. For, as this is nearly null in fever, especially in its relapsing forms, and after the fever only increases very gradually, there should occur immediately after the fever a gradual increase in the amount of urea excreted, which is never the case. VOIT has established that the whole of the nitrogen introduced with the food must make its appearance in the faeces and urine within twenty-four hours, provided that the organism be in a state of equipoised nutrition. This state is not by any means present immediately after the cessation of fever; it is rather to be assumed that the condition then existing is like that following a period of inanition. In such a case the greater part of the food taken is generally used for the replacing of lost elements. If the urea excreted in the epicritic period derives chiefly from the food, then its quantity immediately after the fever must be relatively small, and it must afterward gradually increase. The contrary is, however, the case, and according to

the facts observed, this retention cannot be ascribed to greater drinking of water and consequently increased carrying off of urea. Consequently, the only possible cause of this increased excretion is increased metamorphosis, and, as it cannot be supposed that during the long-continued low, often sub-normal temperature after the crisis, an increased consumption of the constituents of the body takes place, the conclusion is justified that the increased epicritic excretion of urea is the result of the more active chemical changes during the febrile period. R. further states that these increased products of metamorphosis originating during the fever, may be retained in the organism, to undergo a gradual elimination; and thinks that since according to VOIT urea cannot be stored up like chloride of sodium, this law of the normal state is overthrown during and after the fever, or, what is much more probable, that the nitrogenous products of oxidation during the febrile state do not consist of urea alone, but chiefly of its antecedents, creatin, etc.

According to SCHULTZEN (*Char.-Annal.*, XV., p. 168), the last opinion is inadmissible. The assumption of an accumulation of products intermediate between albumen and urea, is justified by no analogy. The natural forms preceding urea are probably the same as those which are artificially obtained by splitting up of the albuminates by means of acids and alkalies (viz., leucin, glycocol, and tyrosin; probably also asparaginic and glutaminic acids); the transition-forms between albuminates and the above substances, which are produced by treatment with acids and alkalies, are substances which have the greatest analogy to the natural peptones, are soluble in every proportion in water, and which have an extraordinarily small coefficient of diffusion. In conditions in which complete oxidation is prevented (acute atrophy of the liver, poisoning by phosphorus) these bodies constitute the ultimate products of tissue-changes, and are excreted through the kidneys just as urea is under normal conditions. If these products are formed in such quantities, during fever, that the process of combustion is not sufficient for their destruction, there must be, in addition to the important excretion of urea, a certain amount or at least a small quantity of these substances in the urine. This is certainly not the case, however, as analyses of the urine show. The conception of an accumulation of nitrogenous forerunners of urea can only be supported by the far-fetched assumption, that wholly abnormal non-diffusible substances are produced in fever. The post-febrile excretion of urea is explained by S. in the following manner: During the febrile state a part of the organ-albumen passes into the circulation, thus entering the sphere of oxidation in the economy, is split up, and oxidized to urea. This is probably due to the destruction of a number of those cellular elements which are looked upon as storehouses for albumen. In the healthy, VOIT's nitrogen-equipoise exists: in sudden increase of the amount of food albumen is retained in the body because the cellular storehouses take up enough albumen to place themselves in equilibrium with the more concentrated surrounding fluids; in diminution of the amount of food, the circulation-albumen contained in the fluids is oxidized, and its diminished concentration causes an outpouring of albumen from the storehouses, the flow continuing until the equilibrium is restored between the amount of albumen in the circulating fluid, and that in the storehouses. The analogue of increased supply of food in the healthy is, in fever-patients, the increase of the circulation-albumen by the destruction of albuminous cells; by which are caused: 1, the increased production of urea; 2, an outpouring of albumen toward unchanged cells, and other albuminous organs. If the fever now suddenly cease, and with it the destruction of cells, a state is produced resembling that present in hungry persons. In consequence of the cessation of the febrile destruction of cells, the production of urea diminishes, but does not suddenly fall to a minimum, but continues for a time tolerably great, because the overcharged albuminous organs must be placed in equilibrium with the circulating fluids before the organism can take up more nitrogen than it can excrete. A fever-patient consequently is just like a person undergoing fattening, but upon the cessation of the fever he resembles a starving one, with the difference, that the fever-patient subsists upon his own materials, and that when the fever ceases this source of food is exhausted.

UNRUH (*Virch. Arch.*, XLVIII., p. 284) considers it probable that for a short time after the crisis increased oxidation of albuminous substances goes on, although the whole amount of urea cannot be thus derived. The assumption of the retention of excretions, or of imperfect products of oxidation, which is rejected by SCHULTZEN, is held by U., in agreement with RIESENFELD, as necessary to the explication of increased epicritic excretion of urea. Besides, U. rejects the hypothesis that this process can be caused by the absorption of an exudation, as in pneumonia, for example, especially as the same phenomenon is observed without preceding exudation, as in exanthematous typhus, erysipelas. Against a possible increased absorption of

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nutriment as a cause, is the very small and not increased excretion of chloride of sodium. WALDEYER (*Virch.-Hirsch, Jahrb.*, 1869, I., p. 236) remarks in this connection that it must not be forgotten that in all acute febrile diseases, even those which seem to go through their whole course without any apparent exudation, a large amount of lymphoid corpuscles is deposited in the various organs and tissues, especially the liver, spleen, kidneys, etc., in certain mucous membranes, and also in the external skin; which exudation is absorbed in the epicritic stage: but as yet there is nothing to indicate how rapidly these bodies are removed from the tissues.

NAUNYN (*Arch. f. Anat., u. s. w.*, 1870, p. 177) finds that the assumption that the post-febrile increase of excretion of urea is to be referred to an over-saturation of the tissues with urea produced during the fever, is not to be rejected as inadmissible, as it has not been shown by investigations directed to this subject that such an accumulation of urea does not take place, or in what amounts it does occur. Up to the present time there is nothing based on facts which can serve as a standard for the determination of the time required for the elimination of the urea produced in organs : neither the processes of digestion, nor the experiments of VOIT on feeding with urea, can solve the question. N.'s experiments with feverish dogs, which, on account of the almost irremediable irregularity of the dietetic conditions in man, and of the very variable amount of aqueous exhalation from the human skin, and the consequent irregularity in the excretion of urine and urea, must be considered as of more value than observations on men,—these experiments indicate that the post-febrile increase of urea-excretion is caused entirely by retardation of the excretion. Their number is too small to decide the question ; but they make caution necessary with regard to conclusions upon the theories of metamorphosis in fever, based upon observations on man.

The fact of post-febrile increase of urea was first determined by BARTELS (*Greifsw. med. Beitr.*, 1865, III., p. 36). B. explained it simply by incomplete escape of the urea formed and stored up in various organs. (He produced the fever in his experiments artificially by means of the steam-bath.)

In a protracted crisis the epicritic increase of urea does not appear so evident, and this is the more marked the more the cessation of fever approaches the type of lysis, when a slow gradual decrease of urea is sooner established. This decrease, in the remittent stage of typhoid fever, in which it is constantly observed, seems to depend in greater part upon the inability of the organism exhausted by continued fever, to oxidize considerable parts of its own constituents, as then the excretion of urea occasionally falls far below the normal amount.

Thus UNRUH has met with an excretion of about 14 grm., and once only 9 grm., of urea *per diem* at the close of a typhoid fever (toward the end of the third week), whereas previously 20–30 grm. had been eliminated.

Observations have also shown that even if under certain conditions during short periods of time the influence of a febrile body-heat upon the excretion of urea is unmistakable, this influence is during the entire course of a fever often concealed by a number of circumstances, and its existence has been seemingly rightly denied. Such circumstances are the original conditions of nutrition and its alterations during the fever, sometimes simply by its long duration, sometimes by a disturbance in the processes of oxidation caused by the fever, as occurs in quick falling of the temperature, and, lastly, by various peculiarities in individual diseases.*

URIC ACID, the nitrogenous ingredient of urine which is next in importance to urea, is also increased in fever, and in about the same proportion as urea ; so much so, that the normal relative amounts of the two substances (1 : 40–70) are not altered. But little can be said with exactness upon the causes of increased excretion of uric acid, because besides the conditions

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* RINGER's researches on the state of the urine in fever (*vide* p. 639) will be found in *Med.-Chir. Trans.*, 1859, p. 360 ; 1862, p. 111. —[ED.]

of nutrition and the other circumstances which influence these paration of urea, there are other influences, such as, especially, the greater or lesser completeness of the oxidation of organic substances, or a relative insufficiency of respiration, causing an independent increase in the formation of uric acid. The causes of disproportion between the supply of oxygen and its consumption may consist in wholly different conditions, and they are not exclusively to be sought for in anatomical alterations of the respiratory organs, or in disturbance of the physiological activity of the motor apparatus of breathing. Factors capable of disturbing physiologically sufficient breathing may consist in peculiarities in the distribution of the blood, and in faults of its composition, and their effects are first made apparent when (as in fever, or severe bodily exercise) the waste of tissues is increased. Furthermore, it is well known that the frequent uratic sediments found in the urine of fever patients, and the deposit of crystals of uric acid do not depend upon increase of production of uric acid in the body.

H. RANKE (*Beob., etc., über Harns.*, München, 1858) estimates the amount of uric acid excreted by a healthy person taking mixed food, at a mean of 0.648 grm. (from 0.455 to 0.875 grm.); and its proportion to urea at from 1 : 41 to 1 : 63. In attacks of intermittent fever he ascertained that there was increased excretion. UNRUH (*Virch. Arch.*, XLVIII., p. 259) found as a maximum, without any distinct disturbance of respiration, 2.169 grm. *per diem :* that is to say, an increase 3.36-fold the normal ; although occasionally there occurred in fever a diminution below the normal, just as in the case of urea. Apart from these exceptions, the limits of increase lie between 1.19- and 3.33-fold the normal ; and the mean of all observations in severe fever gives 0.844 grm. equal to 1.66-fold the normal. Consult especially BARTELS (*Greifsw. med. Beitr.*, Anhang zu Bd. II., p. 15 ; and *Deut. Arch. f. kl. Med.*, I., p. 13).

The remaining nitrogenous ingredients of the urine, creatinin especially, are excreted in greater quantities during fever.

According to KOPPE (*Petersb. med. Zeitschr.*, 1868, XIV., p. 75), the proportion of AMMONIA is increased in febrile states, especially in infectious diseases, the most in typhoid fever. It has not yet been determined whether there are constant differences in the amount excreted in various stages of the disease.

Concerning the MINERAL CONSTITUENTS of urine the following is to be said. In all febrile diseases, especially in the acute, the excretion of CHLORINE diminishes rapidly, and often sinks to a minimum, sometimes so nearly ceasing that hardly a hundredth part of the normal amount can be found. It increases during improvement, and occasionally exceeds the normal in convalescence. The causes of this decrease consist in the lessened and often lost appetite, and in the diet of the sick which contains but little salt ; and at times the formation of exudations and transudations containing much saline matter exerts an influence. These causes also induce a diminution of the amount of saline matter in the blood. Perhaps there is, simultaneously, an impairment of the capacity of the kidneys to separate the chlorides.

An exception to the above rule seems to be in the case of intermittent fever, during paroxysms of which the excretion of chlorides is occasionally much increased. (J. VOGEL, *Harnanalyse.*)

The excretion of PHOSPHORIC ACID also depends partly upon changes in metamorphosis, and partly upon the amount which enters the organism. Occasionally its diminution in severe fever, and especially in short diseases, is insignificant and hardly noticeable. Besides, it is contained in less quantity in the faeces.

The excretion of phosphoric acid, according to MOSLER, varies in the healthy to about 2.5 and 5 grm. *per diem ;* NEUBAUER gives the same proportion. It is distinctly diminished by fasting, food rich in albumen increases it. According to RIESENFELD (*Harnanal. bei Recurrens, Virch. Arch.,* XLVII., p. 130), its amount increases and diminishes with that of urea, as VOIT and BISCHOFF had previously determined. According to ROSENSTEIN (*Virch. Archiv,* XLIII., p. 377) it is very doubtful if fever causes any noteworthy increase of phosphoric acid in the urine.

Concerning the excretion of SULPHURIC ACID nothing precise is known

On the other hand, POTASSA-SALTS are increased in the urine of fever; SODA-SALTS diminished.

According to SALKOWSKI (*Virch. Arch.,* LIII., p. 209), the amount of potassa excreted in a day of fever is 3–4-fold that of a non-febrile day, and this increase may amount to 7-fold what a healthy person on fever-diet excretes. After the crisis the potassa is reduced to a minimum, and a renewed increase is observed during convalescence. The soda behaves in just the opposite way: it diminishes to a minimum during the fever, and increases soon after the crisis, often so rapidly, that on the first day of increase its quantity exceeds the amount excreted on all the fever days together. It, therefore, follows the same changes as chlorine, and for similar reasons. The behavior of potassa is explained by the greater decomposition of potassa-holding tissues in fever (especially the muscles), and also by the destruction of red blood-corpuscles.

Lastly, the amount of CARBONIC ACID in the urine is also increased.

EWALD (*Arch. f. Anat., Phys., etc.,* 1873, p. 1) observed in relapsing fever, typhoid fever, pneumonia, that in the same individual, and under as nearly as possible similar external conditions (diet, rest in bed, etc.), the amount of CO_2 in the urine was increased from 1.2 to 3.3-fold the amount excreted on days of apyrexia; thus making a parallelism between the excretion of urea and CO_2

ALBUMEN is found in urine only in very intense fever, and even then not regularly: its amount is seldom noteworthy. As a rule, it is only after the long duration of such a fever that a moderate albuminuria appears, disappearing after the cessation of pyrexia. This albuminuria is caused partly by altered conditions of blood-pressure, partly by the transitory anatomical changes above described, and it is probable, also, that the diffusion of albumen has experienced a change; though the last is less likely to exist in this form of albuminuria. When the urine contains much albumen, and especially when there is admixture of blood, there is present independent renal disease. As a rule in febrile albuminuria there occurs only a moderate detachment of epithelium from the urinary tubules, causing cloudiness of the urine of pyrexia; and in rather intense grades of fever this may amount to symptoms of a slight catarrhal nephritis, with epithelial and (few) hyaline casts in the urine.

That NUTRITION suffers in febrile diseases, and that in consequence the BODY-WEIGHT diminishes, are facts which have long been known, but which have only been studied and determined with exactness in recent times by regular and repeated weighings. It is a matter of experience that those are exceptional cases in which during a febrile affection the appetite and digestion remain normal, so as to make it possible to make good the waste by increased ingestion of nutritive material. Apart from these cases, there must result, simply from disturbance in the supply of food in fever, a diminution of the tissues of the body, if the appetite and digestion are to various degrees abnormal. Besides, various other causal conditions come into play, such as disturbed respiration, impaired formation of blood, certain exudations and losses of fluids, various local affections, especially those which

cause copious transudation. The influence of all these factors is by themselves only small, but if fever be superadded it immediately becomes potent, and the more so the higher the fever is. Consequently we must attribute to fever a more important influence, even the greatest influence in causing the consumption of the body which goes on during its prevalence. Especially striking is the loss of body-weight in severe acute febrile diseases. This is proven to be, usually, a steadily progressive loss during the duration of pyrexia. In individual cases, it is not always easy to recognize the influence of the fever upon the considerable variations of body-weight which are observed, if we make allowance for the variations which normally occur in the course of the day, and for the accidental circumstances by which it may temporarily be influenced (amount of ingesta, as well as of secretion and excretions) ; and there are some cases of slight fever in which no loss of weight takes place, and in which, for a time, an apparent slight gain occurs.

According to LEYDEN (*D. Arch. f. klin. Med.*, V., p. 368), the following are the variations of the body-weight in healthy persons and convalescents in the course of a day : the least weight is observed in the morning, increases through the day by ingestion of food, reaching a maximum after the evening meal, and falling to a minimum in the course of the night. In high fever the opposite is the case. Then the maximum body-weight appears in the morning hours, grows less during the day, and reaches a minimum in the evening, to increase during the night. L. explains this peculiar condition by existence of great thirst and consequent abundant drinking of water during the night : in the day during the remission less water is needed and taken. Coinciding with this the excretion of water is diminished, or, at any rate, not correspondingly increased.

Furthermore, LEYDEN estimates, on the strength of numerous weighings in various febrile diseases, that the average daily loss of weight per kilogramme of body-weight amounts to :

5.72	per thousand,	in	slight fever.
4.50	"	"	" remission.
10.60	"	"	" the crisis.
5.90	"	"	" the epicritic stage.
2.40	"	"	" the beginning of convalescence.

The factor which undoubtedly exerts the greatest influence upon these results is the exhalation of water from the skin. The loss of weight during the crisis attains to double that in the height of the fever (non-sweating period), doubtless only because of the then extremely abundant secretion of sweat; and the same cause may well determine the relatively high figure in the remission. Even in the epicritic stage, with the continued tendency to perspiration, the loss of weight is as great as during intense fever. The loss of weight continues, though in greatly reduced quantity, during a short period at the commencement of convalescence, although the restoration of the normal physical and chemical conditions of the tissues begins with the crisis, and nutritious food is taken in the course of the next few days. L. explains these differences, which are not to be accounted for by febrile consumption, by assuming that a retention of water takes place in the organism at the height of the fever, and states that this is subsequently removed by increased exhalation of water. He considers, as favoring his view: the small amount of urine which, in spite of great thirst and free drinking, is passed during fever ; the febrile turgescence of the fever-patient's face, as well as the circumstance that it appears most emaciated in convalescence ; and, finally, the demonstrated fact that the blood in fever contains a larger proportion of water. He makes a comparison between the state of the patient before and during the crisis, with the above-mentioned described condition during remission and exacerbation, in which latter so much water is retained that an increase of weight may ensue.

NAUNYN (*vide supra*) also found that a retention of water took place at the beginning of fever, causing, at its height, an increased flow of urine.

On the contrary, according to SENATOR (*Fieberhft. Proc.*, 1873, p. 130), it has as yet not been in any way demonstrated that the body is rendered richer in water by

the febrile process as such, than by similar conditions without fever, *e.g.*, in simple inanition, to which sufficient regard has not been had in the earlier investigations. S. comes to the following conclusions on this subject. An increase of water by oxidation certainly does not take place; its production without oxidation is possible, but has not been demonstrated. The excretion of watery vapor is somewhat increased on the whole during long periods, and about in the same ratio as, or in a little larger proportion than the CO_2; consequently the amount of urine (and other secretions) is smaller. It is as yet undetermined whether during fever there is on the whole more or less water given off through the kidneys, lungs, and skin, than in similar conditions without fever. A fever-patient may retain water just as well as a healthy person, if the loss of water is equipoised or exceeded by the taking of fluid.

According to SCHNEIDER (*Arch. f. klin. Chir.*, 1869, XI., p. 131), in some cases of traumatic fever the fluctuations of body-heat agree with those in health, the minimum occurring in the morning, and the maximum after the evening meal; the taking of food, and the excretions on the whole, are smaller. Of the latter (excretions) the insensible are relatively much larger than in non-febrile states, and indeed their increase exceeds the decrease of the sensible excretions, so that the loss of body-weight in fever is not simply to be explained by diminished supply, but also by the increase of the perspiration.

Even in CHRONIC FEBRILE DISEASES the WASTE produced by the fever is generally easily recognized. As long as the fever is to a certain degree severe, and there are no long-continued intermissions, the decrease of the tissues goes on progressively until death. It is different in moderate fever with frequent intermissions. Thus we not seldom meet with cases which seem to throw doubt upon the general applicability of the law, that fever consumes. In order to understand these exceptions, it is necessary to bear in mind all those conditions which, apart from pyrexia, are capable of affecting the body-weight. It is easy to understand that in some few cases it is not possible to fully appreciate all of these conditions.

Among the local affections which especially influence the body-weight, severe diseases of the digestive organs are to be placed in the first rank: cancer of the stomach, sometimes suppurating, severe intestinal diseases of small children having diarrhœa, cholera. Among losses of fluids, prolonged lactation is one of the most important, supposing that the milk is not suppressed at the beginning of fevers, as is often the case. It is not invariably right to speak of continued suppuration as an exhausting event; this is true only when there is fever likewise. Especially does this remark apply to the loss of fluid by secretion of large amounts of expectoration in consumptives. The wasting of these patients is in much greater part caused by the fever; often the pulmonary disease is insignificant, and destruction of lung-tissue as well as suppuration are wholly absent.

LIEBERMEISTER (*Prag. Vierte'j.*. LXXXVII., p. 11) calls attention to a circumstance which is well fitted to vitiate the results of the estimation of body-weight in patients, and to lead to erroneous conclusions. While, usually, the increase of weight produced by dropsical swelling is not noticeable, it is sometimes so great as to double the weight of the body; and at other times slight œdema of limited parts of the body (not merely of the lower extremities) may be causes of error. It seems to follow from these observations that, in disease, a not insignificant amount of weight may be caused by retention of parenchymatous fluid, without a trace of œdema being present; and these are just the cases in which, in spite of all precautions and attention, false conclusions may be drawn from the results of weighing the body. In chronic cases distinct œdema appears after the lapse of some time, and draws attention to the source of error; but this is only exceptionally the case in acute diseases.

No sufficient investigation has yet been made to determine how much the body-weight may decrease from the beginning of a febrile disease to the

beginning of unavoidable death. Among the difficulties in the way are, that the weight before the appearance of sickness is as a rule unknown, and that toward the close the appearance of œdema not rarely impairs the value of the weighings. The assumption of authors, that 40%, or nearly half the body-weight (perhaps a little more), may be lost before death ensues, appears applicable to some cases; as a rule, however, death is produced by exhaustion before this loss has occurred.

LEYDEN (*D. Arch.*, V., p. 369) estimates the average daily loss of body-weight at .7%; that is to say, at about one-half that occurring in complete starvation (RANKE). But if, according to CHOSSAT (*Rech. expér. sur l'inanition*, 1843), death ensues (in starvation) when 40% of the substance of the body has been lost, then the febrile waste must, in the course of eight weeks, be so great as to cause death by inanition. This agrees quite well with what is observed at the bedside.

LIEBERMEISTER (*Prag. Viertelj.*, LXXXVII., p. 50) finds that the waste, when produced by a chronic fever, may, under certain conditions, be greater than that occurring in simple inanition without producing death. For, as in the latter case the noteworthy fall of temperature which occurs toward the last plays a most important part among the immediate causes of death; the facts are perhaps explained by admitting that this lowering of temperature is prevented by the fever, just as it can be by artificial warming. It is not difficult to admit this, since CHOSSAT states that fever makes it possible to bear such a loss of substance as would be sufficient, in its absence, to produce arrest of heat-production and cause death by refrigeration.

From what has been said in the preceding pages of the conditions of body-heat in disease, its extraordinary importance in the symptom-group of fever can readily be appreciated. Under very many circumstances it is not merely of scientific, but of practical interest, to know the course of temperature, because upon such knowledge we can, in special cases, base the most important and helping measures. In spite of this great importance of a knowledge of temperature-variations, it must not be neglected, in too great confidence in the meaning of this knowledge, to devote care to the observation of the remaining phenomena of disease, and, more particularly, to their agreement or disagreement with the temperature. Their connections may be very various. For: 1. The change of body-heat often depends upon disease of one organ, which offers special symptoms besides: it is thus a consequence of a local disease; 2. It is, further, just like the local symptoms, a consequence of a general disorder, as, for example, an infection or other external influence; 3. If especially great deviations from the normal temperature (highest grade of fever, collapse) of themselves indicate the existence of marked functional disorder, and, when lasting longer, of organic changes, extremely complicated symptom-groups must be expected; 4. Lastly, the influence of countless accidental circumstances must be borne in mind, which may or may not appear in relation to the temperature. In individual cases it is continually to be considered in how much the existing temperature corresponds with the other symptoms of disease. If it is seen to be in harmony with them, as clear as possible an insight into the state of the patient is obtained, and further diagnostic reflection is not necessary. On the contrary, if there be observed a contrast between the degree of temperature and the other phenomena, the greatest importance is to be attached to the changes of temperature, when they are relatively considerable. When the body-heat is less than the other symptoms would seem to require, it must be remembered that there are diseases in which, as we know by experience, severe symptoms may co-exist with slightly increased or normal temperature; or that the disease

may be at the close of a previously more intense course ; and it must be considered that accidental or therapeutical influences may have diminished the fever. If none of the above explanations can be applied to the case, it may be that the reduction of temperature is caused by a complication capable of diminishing the body-heat, or by a commencing collapse.

The contrast of low or of normal temperature, with much complaint of ill feeling, should lead the physician to think of simulation and exaggeration, but also of concealed (latent) chronic changes, or, when the course of the affection is acute, to an insignificant disease, or to such as we empirically know do sometimes develop with low temperature : as diphtheria, renal diseases, moderate pericarditis. The same condition is possible in advanced critical defervescence. Coincidence of high temperature, with good subjective feelings, is not rarely met with in the high fever of several infectious diseases.

A contrast between the temperature and the PULSE-RATE is very frequent. Slight want of correspondence in the height of both is common ; the pulse often following after an improvement in the body-heat, while in worse states it is very likely to advance ahead of the temperature. A low pulse-rate with a high temperature indicates that the nervous system is calm ; it may also be met with under special conditions (as pressure on the brain, action of biliary acids, and of certain medicines). A high pulse-rate may be (rarely) normal to the patient ; it may be due to the influence of muscular movements, and other pulse-exciting influences ; it also may point especially to acute and chronic cardiac diseases, as well as to injury to the heart by morbid states in the thorax and abdomen. Lastly we meet with greatly increased frequency of the pulse, associated in a very remarkable manner with the low temperatures of collapse, and of impending death. In general, when forming a judgment, that factor which of itself gives the gravest indication should be taken as the standard ; the more so, the greater the contrast.

When marked increased frequency of the RESPIRATION appears with moderate fever, we are to suspect a local affection. This increase is often observed in collapse.

Between NERVOUS SYMPTOMS and the body-heat there is sometimes a certain parallelism, sometimes a remarkable contrasting behavior. Children and old people are more irritable than healthy adults : when the former exhibit disturbed functions with a moderate fever, the latter often have undisturbed functions with a highly raised temperature. In this respect, and especially with reference to cerebral disturbance, the individual predisposition plays a great part ; marked brain-symptoms with fever lead to the suspicion of cerebral disease in an adult, whereas in children they in general signify much less. Among others there appear, usually in consequence of inanition and consecutive cerebral anæmia, or slight cerebral œdema, dangerous brain-symptoms with low temperatures, without symptoms of collapse ; especially after severe fevers. These symptoms have, as a rule, a much less important meaning than has heretofore been attributed to them.

The explanation of the connection existing between single local symptoms and the body-heat, concerns special pathology.

B. REGULATION OF ANIMAL HEAT.

One of the most wonderful peculiarities of the human body is that in a state of health, and under ordinary circumstances, the heat of its internal parts is easily maintained at, or about, $37°$ C. This is only possible by the uninterrupted production of heat replacing that which is also equally continually given off ; or in other words, the normal temperature is the resultant of EQUAL SUPPLY AND LOSS OF HEAT. If one of these factors preponderate, the body-heat must vary in a corresponding manner ; and, thus, it rises when the supply of heat exceeds the loss, whereas when the conditions are reversed it sinks. Consequently, a febrile rise of temperature may ensue either when the production of heat increases without there being a corresponding loss of heat, or when the deperdition of caloric is lessened, without there being equal diminution in the production of animal heat.

The essential SOURCES OF HEAT in the organism are exclusively chemical processes, based upon the oxidation of nitrogeneous, and especially of non-nitrogenous substances. The production of heat in an adult during twenty-four hours is estimated at $2\frac{1}{2}$–3 millions calories.* (By the term "caloric" is understood the amount of heat which is required to raise the temperature of 1 grm. of water by 1° C.)

It is well-known that heat is set free if two substances enter into chemical combination. The amount of heat liberated in the combustion

Of 1 grm. C into CO_2 amounts to 8,086 calories (according to FAVRE and SILBERMAN).
" 1 grm. H " HO " 34,462 cal.

The amount of heat produced is the same whether the combustion takes place slowly or quickly, or whether it takes place directly or by means of intermediate steps. However, the rule is generally good, that atoms already in combinations with others produce less heat than those which are free. The following is an estimation of the production obtained from what is ingested by an adult in twenty-four hours:

From albumen............ 599,760 cal.
" carbo-hydrates......1,081,410 "
" fats.............. 816,210 "
————
Total........2,497,380 cal.

The value of the albumen is diminished by the fact that albuminous bodies only half-burnt (e.g., urea) escape from the organism.
LIEBERMEISTER'S unit of heat [KILO-CALORIC] is one thousand times greater: it is that necessary to raise the temperature of 1 kil. of water 1° C.

The production of heat is diminished: by a lessened amount of food, by nitrogenous food, by reduced respiration, as, for example, in sleep, by bodily and mental rest, etc. It is increased: by a greater amount of food, as in winter, by unusual muscular movements, by nervous influence, etc. From its places of origin (the blood and tissues) animal heat is distributed to all parts of the body by the blood. Naturally the heat of any given part depends partly upon the amount of caloric produced in it, and partly upon that which is brought to it. For, as the latter is produced deep in the body (chiefly in muscles and abdominal viscera) it naturally is the chief source of heating for the peripheral parts; since it is as yet impossible to state how much caloric is produced in them (the skin especially).

LOSS OF HEAT takes place principally though radiation and conduction; in much smaller degree by the evaporation of water on the skin and from the lungs; and still less by the heating of ingested materials and of the air inspired, as well as by the expulsion of warmed excretions. The exertion of mechanical labor exerts a variable influence.

Hitherto it has been very incompletely discovered how the loss of heat is divided up among these factors. At all events, by far the greater part of this loss is caused by radiation from the skin. Increased muscular activity does cause a loss of heat; but this is more than compensated by increased consumption and heightened combustion; so that an active body, in mechanical activity, produces more heat than one in a state of rest.

According to HELMHOLTZ'S estimate, the loss of heat from the body is divided up as follows:

* Consult GANOT, Elementary Treatise on Physics, p. 341; Lond., 1872.—[ED.]

Radiation and evaporation from the skin........77.5 per cent.
Heating of ingesta........................... 2.6   "
Heating of inspired air....................... 5.2   "
Evaporation from the lungs...................14.7   "

LUDWIG estimates the amount of heat consumed by mechanical labor at 7 per cent. of that obtained from the food. This loss must not be too highly estimated, because the mechanical equivalent of heat is very large, and because a very great amount of work is required to produce a very small elevation of heat.

It would be of the greatest importance for the knowledge of fever if we could discover a method of directly estimating, with the fewest possible errors, the amount of heat produced in the body and given off from it. This has not yet been possible, because calorimetric investigations, difficult in themselves, meet with special impediments in living beings. Not even has the theoretically incontestable proposition, that all animal heat has its source in those decompositions which are called tissue-metamorphosis, been experimentally demonstrated. Under these circumstances, we cannot speak of physiological data sufficient to account for pathological variations in body-heat.

As the body produces heat continuously, its temperature would necessarily rise if heat were not also given off at the same time. The body-heat can only be maintained at a constant degree as long as exactly the same amount of heat is lost, in a given time, as is produced.

The contrivances by means of which preservation of the normal degree of heat, regulation of heat, is brought about, are very diverse. The mode of operation of some of them is comprehensible; while of others we only know their effect, and we are as yet wholly or in part unenlightened as to the way in which they produce these effects.

Most evident is the regulation of the loss of heat by the skin. If this is decidedly increased by external conditions, as, for example, when the surrounding air is colder than usual, certain agencies become active, and in consequence the loss of heat becomes less than what it would have been without them. The surface of the skin is made cooler, and thus the direct loss of heat by radiation as well as evaporation is restricted, for the cooler skin is less moist. Besides, by the influence of cold, the muscular layer of the skin and of its vessels is made to contract; less blood passes through the skin, and consequently less heat is brought to it from within, and naturally less heat is lost. In this way the reserved amount of heat produced in the internal parts is retained as much as possible by the action of cold. The opposite occurs in warm air. In this case the skin of itself, and also because it sweats, gives off more heat, the blood is driven to the surface, and by enlarging the bloodvessels it facilitates the escape of heat. By means of sweating and of active evaporation of water from the surface, it is made possible for human beings to exist in a temperature which almost or quite equals that of the body.

English observers in 1775 were able to endure for a short time, in a dry air, an atmospheric heat which reached or even surpassed the boiling-point of water (100 C.). Similar examples are given by HOPPE (consult LUDWIG, *Physiologie*, 2 Aufl., II., p. 730).

[An oven, heated to 400°–600° F. (204+°–315+° C.), has been entered. See CARPENTER, *Principles of Human Physiology*, Lond., 1869, p. 484.—ED.]

Experimental facts go to show that there exists in the respiratory organs a mechanism for the regulation of body-heat.

ACKERMANN found that in a dog, whose temperature was raised by exposure of its surface to blood-warm or warmer air, the rapidity of respiration was increased, and the more so in proportion to the elevation of temperature: there ensued a true heat-dyspnœa. If the dog was then rapidly cooled by abstraction of heat from its surface, the former normal respiration-rate reappeared. By means of artificial respiration by means of air having a medium temperature (air of the room), the normal body-heat of the animal was reduced, or if the animal was at the same time kept warm, the rise of temperature was retarded. This, however, did not happen if the temperature of the air administered by artificial respiration was as high as that of the animal. According to GOLDSTEIN (*Ueber Wärmedyspnœ*, Würtz. Diss., 1871), the cause of heat-dyspnœa is in the respiratory centre. G. heated the blood as it passed through the carotid arteries, and by this means the frequency of respiration was much increased; section of the vagi no longer had any influence upon the breathing. Cooling of the blood in the carotids considerably reduced the respiration. FICK (*Arch. f. d. ges. Phys.*, 1871, V., p. 38) observed that in the dog very marked increase of the general temperature and of the heat of the blood in the carotids, which caused great excitation of the respiratory centre, exerted no influence upon the centres of cardiac and vascular innervation.

Just as in heightened external temperature with normal production of heat, the superfluous caloric furnished by increased production, for example, by unusual muscular activity, is at once removed, without there being any remarkable or permanent increase of the body-heat in the healthy individual.

The dispositions already mentioned are without doubt sufficient for the conditions which arise in the normal state, with respect to production and loss of heat, and in the regulating organs as well. Probably they are also sufficient under normal conditions, so that the requisite average is most easily reached from *plus* and *minus*.

It is not unlikely that, while in general the cooling of the organism is done by the skin, the respiratory organs, owing to their condition of ventilation, are better fitted to execute the need of the moment, and thus to equalize the slighter fluctuations in the vicinity of the normal; and that they may, under certain circumstances, act as supplemental to the skin. Nevertheless, the skin itself possesses contrivances by means of which a delicate regulation of the loss of heat can be achieved. For example, if a partial heating or cooling of the cutaneous surface be produced, we can distinctly observe in the first case a rapid increase, and in the second case a decrease of the afflux of blood, and of the local heat in parts of the skin somewhat removed from the locality operated upon. The caloric which is withdrawn or retained in one part by the contact of a cold or of a warm medium, is economized or expelled in some other part.

It is, however, to be observed, that in man the amount of normal variation exists under the operation of numerous external, and to a certain extent controllable factors, as clothing, ingestion of food and drink, muscular activity; in short, external or, perhaps more properly, instinctive suitable means of retention, serve to maintain the normal temperature. Not of itself alone, without help from outside, does the organism determine the normal temperature of the body; the various changes in the amount of blood and the activity of the skin and lungs are not the sole means of correction, but numerous other external aids are required. Their influence upon the amount of production and of loss of heat can neither be calculated nor estimated. "The fact of there being a normal temperature simply indicates that the functions of the healthy warm-blooded organism are only compatible with the temperature specified."

BERGMANN had already said in 1845 (*Müller's Arch.*, p. 310): The skin affords great facilities for phenomena of changes in vascularity, and is thereby well fitted to

assist in equalizing the internal temperature. If the external temperature rise, the temperature of the skin becomes greater, and thus a corresponding derivation of heat can take place. If it (the external temperature) be still higher, or if there occur an increased production of heat at the same time, increased evaporation co-operates to bring about the same result. If the production is increased by internal causes, taking of food, drink, etc., the same series of phenomena may follow without any change in the external temperature. The contrary is to be said of lessened production of heat with and without lowering of the external temperature. It is of course understood that besides these factors, there is the greater sensibility of the skin which leads man to cover himself more, or to do the opposite, as well as to do many other things which might be mentioned, and that every variation in heat of skin and in evaporation must serve to correct errors.

SENATOR believes that the capacity which warm-blooded animals have of maintaining their body-heat at a constant height is really limited to overcoming a difference of a very few degrees, and is founded chiefly upon the property which the skin has of restricting the influence of variations of external temperature to itself, and thereby shielding internal parts. In man there is a latitude, in this respect, of from 8 to 10° C. of atmospheric temperature, within which the organism maintains its proper heat without any external aid. The upper limit of this is at a point not at all higher than the temperature of the blood (37° C.), but rather a little below it; its lower limit is at about 27°–28° C., both being thus estimated with the assumption of average atmospheric pressure and average atmospheric moisture; with changes in these there occur corresponding variations in the evaporation of water. (*Virch. Arch.*, XLV.)

ACKERMANN (*Berl. klin. Wochenschr.*, 1872, p. 26) considers it possible that "under normal conditions," with bodily rest and a medium temperature of the surrounding air, the mean heat of the body will be maintained at a very steady and regular height. Numerous facts, however, indicate that the body-heat by no means remains within normal limits, as soon as important influences, such as those brought about by "instinct," by "unconscious volition," intervene. Animals best preserve their warmth when lying on the belly, or drawn up in a heap, by which means the belly is covered by the ground or by the limbs. If rabbits be tied down upon their backs in an extended position, and left under the influence of an ordinary room-heat, they continuously grow colder, with such rapidity that they die in half a day or one day. This cooling is not a consequence of the fettering of the animal, since it does not take place if it be inclosed by warm covering. Similarly there is undoubtedly more heat given off from the anterior part of the human body than from its posterior surface, and the former requires more protection than the latter, etc.

On the contrary, it appears to LIEBERMEISTER (*Volkm. Samml. klin. Vorträge*, p. 117) "one of the most wonderful provisions in the wonderful arrangement of the human body, that as long as it is healthy, its temperature should remain under all circumstances constantly at (about) a height of 37° C. Even under extremely different circumstances the body-heat remains constant."

According to LIEBERMEISTER, a regulation of heat takes place, "naturally operative only within given physical possibilities," especially the regulation of production according to the loss, in a reflex way, and indeed under the operation of two separate systems, "an excito-caloric, and a moderating system," both of which have their centres in the brain. Because by a separation of the brain from its nervous connections with the rest of the body, the previously steady temperature becomes wholly changeable, and wholly dependent upon the amount of heat lost, it appears probable to L. that this connection is a condition necessary for regulation of the production of heat. The immediate diminution of body-heat which occurs in animals after the section of the upper part of the spinal cord (NAUNYN and QUINCKE), even with moderate loss of heat, as well as under conditions in which, without operation, the loss is compensated by an immediate proportionately increased production of heat, and also the phenomena in a healthy person in the cold bath, which are of "variously active character (increase of heat and greater production of CO_2 to three or four-fold the normal amount)," very surely indicate the existence of an excito-caloric system: excitation of certain nervous paths by the irritation of cold accelerates the processes of oxidation. On the other hand, according to L., facts also speak for the existence of a moderating system, whose inhibitory influence is removed by section of the spinal cord, leading to the immoderate production of heat. In the normal state there occurs under the operation of this system a moderation of the loss of heat and a small production of heat, which are all the greater the higher the temperature of the skin is; and *vice versâ*. The assumption of the existence of a moderating apparatus is supported by the considerable increase of temperature which is sometimes observed in man after injuries to the spinal cord, as well as in larger animals after its section;

and, lastly, by the observation of TSCHESCHICHIN, according to whom even in small animals the body-heat rises much and steadily after the pons has been separated from the medulla by section.

It has been attempted, by various means, to acquire a more exact knowledge of the amount of production and loss of animal heat. In the last few years the influence of removal of heat by the skin has been made use of for this purpose.

Formerly it was thought that the operation of losing heat was exclusively due to changes in the peripheral circulation, and it was assumed that it was also possible, by volitional, semi-volitional and instinctive means (food, exercise, etc.) to protect the fixed normal temperature of the organism from the effects of moderate changes of external temperature. Of late years, however, the opinion has been brought forward that the organism, within certain limits and in a wholly involuntary manner, regulates its production of heat in accordance with the peripheral loss, and that, as an immediate consequence of every withdrawal of heat and in exact proportion to its amount, the processes of oxidation in the body are made more active.

As regards the immediate effect of removal of heat, the first effect of such an action, as in the case of the refrigeration of the exposed skin of man (if not too slight), is found to consist in a nearly simultaneous or quickly following rise of temperature in the axilla, much smaller in proportion than the preceding diminution, and somewhat later in the rectum a slower lowering of temperature; seldom no change. In animals the manifestations vary according to their size: small animals, as rabbits, which have relatively a much larger surface, show a continuous fall of temperature; larger dogs not seldom exhibit a rise of temperature in the rectum, analogous to that in the axilla of man. There seems to be, in larger animals and in man, between the considerably cooled external parts and the less and more slowly cooled internal parts, a layer in which a slight increase of heat takes place. In prolonged, and more especially in greater abstraction of heat, the temperature of this intermediate region, as indicated by measurement in the axilla, ultimately falls and does so continuously as long as the experiment can be continued without injury to health. This may be observed, for example, when the subject is placed naked in a cool bath or exposed to a low temperature, etc.

SENATOR (Arch. f. Anat., Phys., etc., 1872, p. 35) explains these phenomena as follows. He looks upon the effect of intense refrigeration as made up of the effect of a strong irritation of a large number of nerve-endings, and of the effect of withdrawal of heat. This at first affects the peripheral layers. Strong sensory irritation (and cold is one of the most active and persistent irritants) produces a narrowing of the bloodvessels in the irritated region, and, also, a reduction of the internal temperature. This latter distant result he, with HEIDENHAIN, explains by the supposition that the vessels of the subcutaneous layers of connective tissue and muscles enlarge under increased blood-pressure, in consequence of which the rapidity of the circulation increases, and more heat is sent from the deeper parts to this middle layer, causing an increase of temperature. A much more important rise of temperature is due, however, to the circumstance that by the contraction of the bloodvessels of the skin and of the cutaneous muscles, the specially heat-producing part of the body is more or less completely deprived of the means of getting rid of its heat (especially in a bath, which prevents evaporation from all parts which are wet), and this must accumulate in those tissues which lie next under the skin, and whose vessels have been enlarged. Whereas the provision of heat in the internal parts remains protected, and is at the most a little cooled by the blood coming in from the periphery, the middle layer (that of the muscles) gains heat in a double way, chiefly because it gives off less, and also because it receives a supply from within: there occurs in it an accumulation of a great part of the heat of the organism. This accu-

mulation is gradually equalized, however, as well by the penetration of the cooling into the deeper parts, as by further (though much less) accumulation of heat under the muscular layer which was first heated : it gains this more by economizing on the skin than in any other way.   Naturally all spots in these various layers do not always behave in the same manner, for various degrees of vascularity and various extent of surface in the different parts must lead to the production of differences in tempera-ture : in the extremities, for instance, the contraction of bloodvessels retards cooling only in a measure, but leads to no heating as in the internal parts.   Lastly, if the cooling exceed the heating in all parts, so that it (the cooling) penetrates directly inward from layer to layer, and that by means of the circulation constantly increas-ing quantities of cooled blood are forced into the internal parts, the temperature of every part is at length lowered.

WINTERNITZ (*Virch. Arch.*, LVI., p. 188) is of the opinion that under otherwise similar conditions the change in the distribution of heat in the organism after refrig-eration (as indicated by differences of temperature in the axilla and rectum) is so much the greater the more mechanical irritation is added to the thermal.   Under similar mechanical influences the operation of refrigeration by means of a low tem-perature produces a greater effect than by means of somewhat higher temperature. The effect of a dry rubbing alone, which is only a mechanical irritation, is less than that of a combination of thermal and mechanical influences, but shows itself in a similar manner ; the temperature of the rectum falls, that of the axilla remains sta-tionary or rises.

LIEBERMEISTER has propounded and very persistently maintained an altogether different interpretation of the observed phenomena.   Whereas SENATOR explains the rise of temperature in the axilla (as well as that of slighter degree in the rectum) which appears at the beginning of refrigeration, without production of heat, by sim-ple accumulation of heat, the assumption of an essentially uniform production of heat independent of loss of heat, does not seem to him well-founded, even in the normal state.   The hypothesis that all the different contrivances, independent of one another, which concur in the mechanism of loss of heat (" they are in part founded upon physical conditions ; in part the complicated structure of the skin, and especi-ally the state of the circulation, of perspiration, and of evaporation at different tem-peratures, in part are the result of instinctive and volition actions on the part of the individual ") under all circumstances co-operate in so precise a manner that the sum-total of all the effect amounts to just enough to make the loss of heat equal to the production of heat :—this hypothesis appears to him inconsistent.   Could such a con-dition be thought possible under normal circumstances, it must appear wholly impos-sible under altered external conditions.   These phenomena L. attempts, in his inter-pretation, to explain by the effect of refrigeration upon the organism.   He does it in the following manner.   If a healthy individual takes a cold bath, provided that its dura-tion be not too long, the temperature of his internal parts is, according to measure-ments taken in the axilla and rectum, not lowered, but it remains unchanged or shows a slight increase ; only after a longer bath in the case of individuals having little power of resistance (only later in others) does the body-heat fall by a few tenths of degrees in the course of 20 or 30 minutes.   As it seems to L., the provision of heat inside the body is not diminished by a cold bath of moderate duration, that is to say, under conditions in which an immense amount of heat is withdrawn from the body.   " Man possesses the inexhaustible oil-bottle; he may pour out as much as he pleases, it remains filled to the same height." (*Volkm klin. Vorträge*, No 19.)

LIEBERMEISTER obtained " unequivocal " results from his experiments.   For exam-ple, if a man heated 160 kil. of bath water from 20.1° to 20.6° C. in nine and a half minutes, a correcting experiment showed that heating would have been 0.03° C. greater if the water had not given off heat to the surrounding air.   Thus the 160 kil. of water were made warmer by 0.53° C., and consequently the body had given to the water $160,000 \times 0.53 = 84,800$ calories.   Under ordinary conditions about 13,000 calories would be given off, so that the loss of heat was about six and a half times greater than the normal amount in the bath.   And in this the heat which, during the bath, is given off from parts of the head not under water and by the respiratory pro-cess, is not reckoned ; this amount is, however, unimportant, and may be left uncon-sidered.   Entirely similar were the results of other experiments, in which the duration of the bath was prolonged to twenty-six and thirty-five minutes.   L. found that in a bath whose temperature was 22.5° C., the loss of heat was four and a half times as much as the usual loss out of a bath; in one of 25° C., more than three times, and in one of 30° C., double the amount   An explanation of these facts seems to L. possible only by assuming that the organism produces, during the whole duration

of the bath, enormous quantities of heat over and above its normal measure, and thus constantly replaces the enormous losses.

Of course the superficial layers and the peripheral parts of the body really become cooled, but the state of the internal provision of heat undoubtedly remains the same. The loss of heat takes place during the first few minutes of the bath, reaching a very high degree, and taking place for the greater part at the expense of peripheral portions, which lose heat without having it fully restored. Thus the total loss of heat observed is not to be considered as simultaneously produced, but that part of it which represents "peripheral refrigeration" is lost without being replaced by contemporary production. The amount of this share may, according to L., be easily ascertained with sufficient accuracy by experiments; and if it be subtracted from the total loss of heat, there remains the amount of heat which is replaced by production. This remainder consequently represents the amount of heat produced during the bath.

In order to be able to estimate the amount of "peripheral cooling" correctly, the temperature of every different part of the body must be exactly known at the beginning and the end of the bath. Since this is not possible, we must be content with taking the temperature of some specified parts. According to LIEBERMEISTER, "the source of error from the above nearly disappears if we consider as the commencement of the experiment not the beginning of the bath, but a time a little later. If once the cooling of peripheral parts has to a certain extent taken place, then a further loss of heat, which shall not have been replaced by production, cannot ensue without producing a diminution of heat in the deeply-lying parts accessible to measurement. How long a time must be allowed to pass before this stationary relation between the temperature of the various parts of the body becomes established, cannot be determined *a priori*, but must be calculated from the results of experiments: these indicate that it occurs in a moderately short time. " During the first minutes of the bath, proportionately more heat is given off from the peripheral parts of the body to the water; after the ebbing of this loss the quantities of heat given off in equal periods of time are about equal, and, in two experiments, even in a duration of seventeen and twenty-six and a half minutes. For, as during this period the axillary temperature does not fall, but shows an insignificant rise, it seems right to conclude that in still deeper parts the body has undergone no cooling. The cooling has consequently affected only the peripheral parts, and occurs, as shown by the quantities of heat received by the water, only during the first minutes. In the whole of the succeeding time, just as under usual conditions, the loss of heat approximates to the production of heat, and therefore the figures representing the loss of heat may be considered as representing the amount of heat produced." According to this method, L. found that during a quiet stay in a bath of 20 –21° C., the production of heat was four-fold; in one of 22 –25 C., three-fold; in one of 30 C., quite double the production which takes place under normal medium conditions. (*Arch. f. klin. Med.*, V., p. 219.) KERNIG's researches, carried out in the same way, showed that in a warm bath of 34 –35 C., the production of heat is about the same as under normal conditions.

Even if, as above indicated, undoubted facts have been demonstrated in various ways, their physiological explication still remains exceedingly variable: according to one opinion there is accumulation of heat without production, or at least without noteworthy production; according to another view, this is undoubtedly much increased. The solution of this question can only be obtained by exact calorimetric investigations.

SENATOR (*Arch f. Anat., Phys., u. s. w.*, 1872, p. 1) studied, by means of a calorimeter which indicated with great exactness the loss of heat from a tin box containing warm water, the production of heat in dogs under various conditions, and particularly under refrigeration. The result of many experiments was, that the animal experimented upon did not, during refrigeration, produce more, but, on the contrary, less heat than is normal, while other experiments made it probable that the production of heat was at least not much increased. The refrigeration was sought to be obtained by having the water of the calorimeter colder than the degree which he had determined by previous experiments to be necessary to the preservation of the normal state: the animal thus being made to sit in the midst of a current of air in an insufficiently warm space. The refrigeration may accordingly be designated as moderate. The results were the same as those observed in man under similar circumstances, for whom LIEBERMEISTER (*Arch. f. Anat., u. s. w.*, 1851, p. 41) made the following estimate: that there were produced per minute 2.7 kilo-calorics by the immediate contact of air

at 12°–22° C. with the surface of the body, whereas under ordinary circumstances only 1.8 kilo-calories were thrown off on the average. L.'s calculations thus were decidedly in favor of an important increase in the production of heat. SENATOR adds to this, that from several facts it must be concluded that the production of heat during refrigeration obeys the same laws in man and in dogs.

For, in all his experiments, even when the duration was only half an hour and the temperature of the calorimeter a relatively high one, when the temperature of the body (measured in the rectum) had sunk, it was possible to object that (what is in itself improbable) the kind and duration of the process of refrigeration, in spite of its apparent insignificance in comparison with sponging and cold baths, had exceeded the limits within which LIEBERMEISTER's regulatory increase of production of heat takes place, and that with yet shorter experiments a positive result, rise of temperature in the rectum, might be expected. But shorter experiments gave no certain results because of the want of standards to measure the changes in the stored-up heat, and are consequently useless.

In opposition to this method, nearly free from error, the theory of the increase of production of heat in proportion to the loss of heat, rests upon much more uncertain grounds. As above stated, the estimation of the amount of production by means of measurements of the temperature of the water of a bath, upon the supposition that an increase of body-heat observed in the axilla or rectum during the period of accumulation of heat, indicates a corresponding increase in the whole body. The most careful consideration here reveals the circumstance, that unavoidable errors in reading off the thermometer may greatly alter the results of calculation, because in the slight increase in the heat of the bath-water and of the parts of the body observed, may even in favorable cases be relatively important. Besides, the above-named assumption is incorrect, and thus an exact estimation of the amount of heat given off to the bath-water is quite impossible.

WINTERNITZ (*Oestr. Jahrb.*, 1871, p. 180) has shown, and ACKERMANN (*Berl. klin. Wochenschr.*, 1872, No. 3) confirmed the fact that the water of an open bath may show in its various strata differences of temperature amounting to several tenths of a degree, and that in spite of a previous thorough mixture. If the heat given off from a mass of water left to itself is not the same from minute to minute, it must be still less so in the case of a living body, especially if it be exposed to energetic refrigeration. In such a case the amount of heat given off to the water in its various strata necessarily fluctuates from minute to minute, and because of the great probability of notable differences between the two factors of the observation, it becomes impossible to draw correct conclusions as to the degree of cooling of the water during the time of bathing, especially if there be a large quantity. The calorimetric apparatus made use of by SENATOR in his experiments gives far more exact results, because the water in it is as much as possible protected against evaporation, conduction, and radiation.

Still more questionable is LIEBERMEISTER's opinion of the constancy of the temperature of the internal parts, " as indicated by measurements in the axilla and rectum," during refrigeration of a healthy animal. When WINTERNITZ plunged one forearm up to the elbow in water colder than the skin, there was soon made manifest a dissimilar course of temperature in both axillæ, which previously had, without such provocation, shown differences of from 0.1 to 0.2 C.; and the rule was that the heat of the axilla on the side opposite to the immersed arm rose in a relatively marked manner, while that of the axilla corresponding to the cooled arm rose but little, remained the same, or even sank. In this way differences of 0.8 C. were produced. Similar variations were produced by immersion of the arm in water warmer than the skin; and even simple friction of one forearm, without exposure, sufficed to cause an increase of 0.1 to 0.2 C. in the axilla of the other side.

New experiments in one case (*Virchow's Archiv*, LVI., p. 182) taught WINTERNITZ the following. Exposure of the body (the effect of a cool chamber air, and wrapping in cool woollen covering being considered) produced in twenty-seven minutes a rise of axillary temperature amounting to 0.49 C., a depression in the rectum equal to 0.3 C.; so that the latter, after the lapse of this time, had a lower temperature than the former, though it (axilla) was 0.65 C. the colder before the experiment. More con-

siderable refrigeration (wet sponging, the air-bath) rendered the reversed progress of the temperature still more striking in both places, the difference in favor of the axilla amounting to 0.4° C. at the end of the experiment.

SENATOR has made analogous observations ; compare what has been said *supra* about the effects of refrigeration. Later he found (*Virch. Arch.*, L., p. 368) that by simply uncovering one half of the body, the temperature of the axilla on the cooled side alone rose, while that of the opposite axilla sank.

ACKERMANN found that if a thermometer is introduced through the jugular vein as far as into the inferior vena cava, and a local cooling application is made on the external skin, the temperature of the blood in the vena cava at once falls, and shows a number of fluctuations, none of which attain the height of the primary temperature. This diminution lasts a little while longer than the cold application. Thus proof is afforded that at least in the middle part of the vena cava the blood is made cooler by external refrigeration (*Berlin. klin. Woch.*, 1872, p. 25).

On the basis of these and of other physiological observations which are not here considered, it is in part demonstrated, in part made probable, that during refrigeration the temperature of internal parts may be very various, and that it is unallowable to look upon the measurement of the temperature of an axilla, or of a part of the rectum, as giving the mean heat of the internal parts of the body. Above all, the heat of the internal parts in general must not be inferred from the great differences in the heat of various organs.

It follows from what has been said, that the assumption that the production of heat is not influenced or at least not much increased by refrigeration, is much more probable than the opposite view, which claims that there is an immediate marked increase of production when the peripheral parts are cooled. If the latter were correct, the loss of heat would be at once actually replaced, so that under all circumstances the temperature of any given part of the interior would remain as high as before the cooling, which in reality is not the case. The lowering of temperature in the rectum at the same time that the heat of the axilla increases, is opposed to the existence of any marked increase in the internal parts. Still more positive is the dissimilar condition of the two axillæ observed under certain circumstances. In this case it cannot be alleged that the increased production of heat shows itself only in the axilla on the cooled side, but is not sufficient to warm both axillæ, or at least to preserve them from cooling. If in this different condition of the two sides of the body the influence of heat-production be not recognized, but only that of various states of blood-vessels, it may be added, at any rate, that there are refrigerations of not less intensity whose effects extend as far as the most distant axilla, and which exert no influence whatever upon the production.

All irritations of the skin (and refrigeration is one) produce a change in the bloodvessels of the affected parts of the body, at first a contraction of the vessels of the skin checking the giving off of heat; though very soon after, especially with strong irritations, there appears a vascular relaxation favorable to this loss, and in consequence the body-heat is lowered. Direct experiments have shown that the giving off of heat by the skin, during very small fluctuations in its surface-temperature, can vary as much as 40% according as the vessels are dilated or contracted. Thus the increased temperature of the axilla, or its constancy, after cutaneous refrigeration of not too long duration, may be explained, without supposing any increased heat-production. In case of longer acting refrigeration with similar effect of the temperature, it is to be considered that there are muscular layers in the neighborhood of the mercurial bulb, the bloodvessels of which (as made very probable by recent researches) do not contract upon the irrita-

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tion of cold on peripheral parts, any more than they do upon irritation of the spinal cord. On the other hand, the internal organs are somewhat cooled by the intense action of cold, partly because their blood flows out toward the muscles (animals killed under such circumstances exhibit internal anæmia), partly because the cooled blood re-enters their vessels. A complete proof of the correctness of this opinion cannot be given at the present time, because we cannot now estimate, on the one hand the products of increased metamorphosis, on the other those of decreased metamorphosis, and also the individual factors by means of which the essentially unknown result is brought about. The chief importance is always attached to the altered distribution of blood, and this, on the principle that where there is less blood, heat is less, and *vice versâ*—with respect to altered function and heat-production in the various organs; according to this, however, a repeated increase of heat-production becomes very doubtful.

It is highly probable, from the results of various observations by WINTERNITZ, that the blood driven out of internal organs flows into the muscles and thus makes in them a warm layer, in which increased production of heat takes place, and by which the internal organs are as far as possible protected from refrigeration. The amount of the compensation thus produced cannot at the present time be approximately estimated, and thus a calculation of the amount of heat-production is made impossible. So long, consequently, as the mechanism of compensation maintains the equilibrium between loss of heat by refrigeration and increased production of heat in the muscles, the axillary temperature will not fall, while the rectal temperature has already fallen because of diminished production; but if the refrigeration be too great the compensation is insufficient, and the axillary temperature falls likewise. Its falling after the cessation of refrigeration is the expression of the equalization of the deranged distribution of blood; and for a similar reason the temperature of the rectum may be even more depressed. Owing to this compensation (increased activity on the one hand, diminished activity on the other), the general balance of the economy is not at all or not specially disturbed; the total consumption may remain the same in spite of increased consumption in one organ, or in a group of organs.

ROSENTHAL finds that an alteration in the production of heat by the effect of variously higher surrounding temperatures is not proven. According to him, all phenomena of the regulation of heat can be explained by the changed giving off of heat from the skin which occurs under various circumstances, produced by changing states of the cutaneous bloodvessels; and next to this, the other regulatory means, such as respiration, evaporation of water, etc., play only secondary parts.

Recently, proceeding upon the correct premise, that increased metamorphosis must cause increased production of heat, it has been proposed to solve the question, whether refrigeration does not cause increased production, by estimating the amount of CO_2 excreted. But such experiments do not give exact results. For we do not yet know the influence of different temperatures upon the excretions of CO_2 from the blood and organs with enough exactness to enable us to conclude from an increased excretion and nothing more to increased combustion. At all events it is imaginable, though at the present time little probable, that under the influence of refrigeration larger amounts of CO_2 pass from organs into the blood, and are given off from the latter to the external world.

According to LIEBERMEISTER, numerous experiments favor the view that under the influence of cold on the organism CO_2 is excreted in larger quantities in consequence of increased heat-production. "The amount of the excreted CO_2 increases if we undress in a chamber whose air is at an ordinary temperature; the increase is greater if the bare body is washed with cold water; and in the cold bath it reaches an extraordinary quantity. For instance, a man who, under ordinary circumstances, excretes about 13 grm. in half an hour, will lose 39 grm. in the same length of time

if placed in a cold bath. Besides, older observers had already frequently noted the fact that with a low temperature of the surrounding air, the excretion of CO_2 is greater than with a higher temperature. (*Volkman's klin. Vorträg*, No. 19.)" "In general, the production of CO_2 is so much more marked the greater is the refrigeration " (*D. Arch. f. klin. Med.*, X., p. 101), and it is besides very possible that this increase of excretion continues for 15–20 minutes after the bath (GILDEMEISTER). SENATOR, however, does not acknowledge such a result upon the basis of his own calculation, but rather intimates that the increase of CO_2 observed by L. is not nearly as great as it should have been, according to L.'s conclusions. The estimation of the amount of heat developed in relation to the increase of CO_2 is always too great to make carbonic acid a standard measure for the conditions of the liberated forces, in which mechanical labor must be included. Even in the state of absolute external rest (so-called) some labor is involved, inasmuch as all the voluntary muscles are never absolutely inactive ; and the muscular apparatus of the excretory ducts of glands, that of the respiratory, circulatory, and digestive systems, works uninterruptedly, and that without externally appreciable movements. Most of these active processes are increased by the irritating effect of cold, and by that alone the production of CO_2 is increased out of proportion to that of heat. The respiratory movements, in particular, become more frequent and energetic under the influence of cold ; and in consequence of this the blood, through greater ventilation, gives off more CO_2, an excess which becomes important for short periods of time (as *e. g.*, in L.'s observations) ; and further, there is greater muscular activity, and more CO_2 is produced. According to P. HERING, two strong expirations, sufficient to produce apnœa, removes nearly all the CO_2 from the blood ; and similarly by the irritating effect of cold during refrigeration the frequency and depth of the respirations are very much increased, and thus the pulmonary ventilation is made so much more active. So that, under the above favorable conditions, an excretion of CO_2 in disproportionate quantities may very well take place without there having been any marked increase in the production of heat at the same time. Consequently, S. concludes that by refrigeration of the surface of the body a considerable increase in heat-production can hardly be said to be produced ; a small increase may naturally be brought about by greater force of respiration, perhaps by altered conditions of friction within the bloodvessels, by a somewhat greater metamorphosis in the heated parts. At any rate, the proposition that the formation of CO_2, and with it the production of heat, is increased by refrigeration, is not yet established.

With respect to urea and uric acid, the experiments referred to as instituted for the special study of fever, have as yet indicated nothing certainly favorable to a regulatory increase of production.

From the investigations made thus far, it results that, with respect to the effect of refrigeration, we must accept the fact of a certain resistance of the internal temperature during moderate duration of the cooling, without there being a generally accepted explanation of it. However, the hypothesis, according to which the preservation of the internal temperature is brought about by a special complex regulatory mechanism, and not simply by changes in the cutaneous bloodvessels, is wholly improbable.

It would appear that the organism shows a smaller resistance against the external influence of heat than against losses of heat which do not exceed a certain limit. The regulatory processes which have their seat in the skin much more easily become relatively insufficient in case of checking of loss of heat, and there consequently ensues an increase in body-heat. Thus, by checking of radiation and evaporation, as in a steam-bath, for example.

In the imperfect state of our knowledge of the nature and mode of action of so apparently simple an interference with the regulation of heat, as refrigeration under physiological conditions, and with the so various significance of the phenomena observed, it is not surprising that the same observations and experiments made in fever-patients have not afforded a clear result, and a nearer insight into the nature of fever. At least, opinions which are held by some, on the strength of their own experiments, to be undoubtedly correct, are by others rejected as utterly untenable.

In particular, LIEBERMEISTER and his school consider the excretion of carbonic acid, occurring when the external skin is cooled, as evidence of the regulatory processes which are active in fever also. (*Volkmann's Samml. klin. Vort.*, V., p. 132.) SENATOR expresses himself as decidedly opposed to all such statements, since increased excretion does not permit us to conclude that there is simultaneous increased production. In opposition to refrigeration by cooling of the skin, there does not take place, according to LIEBERMEISTER (*Ib.*, p. 254), in the case of internal cooling (cold drinks, swallowing of ice, cold enemata), a regulatory increase of heat-production. If it were thus possible to withdraw large amounts of heat from internal organs without great difficulty, this mode of refrigeration would be the one most recommended by theory, since in this way there is no resistance to be overcome, and the organism is not thereby excited to greater production. Nevertheless, practical experience does not appear to favor this opinion. KEMPERDICK (*Berlin. kl. Wochenschr.*, 1873, No. 10) obtained in typhoid fever a marked cooling by the passage of a continuous stream of cold water in the rectum, during several hours, by means of a double canula introduced into this cavity. As the first and immediate effect of this procedure, there occurred, however, a rise of the axillary temperature amounting to 0.2 –0.4 C., that is to say, the same phenomenon as appears when the skin is cooled, and which is to be explained in the same (above explained) manner (that is to say, not in LIEBERMEISTER's way). SENATOR also saw the temperature of the axilla rise in the course of ten minutes from 38.3° C. to 38.55° C., during injections of ice-water in the colon against ileus. The fact that the action of cold from within the stomach does not, as a rule, produce a rise in the axillary temperature, as occurs at the beginning of cutaneous refrigeration, he explains simply by the occurrence of much less sensory irritation, partly because of the much smaller extent of surface, partly because of the degree to which the gastric mucous membrane is accustomed to cold drinks.

Of much greater importance for the acquisition of a nearer insight into the febrile process, than the variously interpreted experiments upon the effect of refrigeration, are the DIRECT EXAMINATIONS OF METAMORPHOSIS in fever-patients.

As the most important facts ascertained with reference to this have been laid before the reader in preceding sections, it only remains to give a short summary of the results: reference is made in the following sections to some few particulars.

Without any doubt, metamorphosis is increased in fever. There does not, however, occur a simple and uniform increase of the normal processes of metamorphosis, but the process of oxidation of nitrogenous substances is made more active than that of the non-nitrogenous.

More especially there occurs a greater destruction of albumen, chiefly indicated by increased excretion of urea, and that in spite of the fact that the conditions for its separation are less favorable in fever, because of diminution in the amount of urine. Even under the most unfavorable circumstances we find in fever-patients an average increase in the excretion of urea, amounting to more than double what is thrown out in non febrile states under otherwise similar conditions. Frequently, almost regularly, the amount of urea begins to increase before the beginning of the fever proper, at least before the chill and rise of temperature. At all events, the destruction of albumen is even greater than is represented by the amount of urea, which is its most important product, and consequently it amounts to more than twice the normal destruction. The nitrogen can leave the body by many other ways, directly as albumen, blood, as ammonia, uric acid, and other products of incomplete oxidation; partly through the urine, diarrhœas, sweat, expectoration, exudation, etc. Those nitrogenous principles which are rich in potassa and blood-pigment (blood-corpuscles, muscles, parenchymatous degeneration of organs) are decomposed in greatest amount.

The provisions for the excretion of CO_2, the most important product

of the decomposition of non-nitrogenous substances, are more favorable in the febrile than in the normal state; and as the excretion is increased by 30–40% in favorable cases, there must occur a slight increase in its formation. This, however, holds good only for the day-time, for then (just as shown by physiological observations in the normal state) it presumably diminishes.

According to a number of investigations, it is the red blood-corpuscles, that is to say, those elements which we know to take up oxygen from the air and serve to transport it to the tissues, which suffer the most in fever. If the organism in fever cannot appropriate as much oxygen as in the same dietetic conditions in the non-febrile state, it likewise cannot furnish as much of products of oxidation. But as larger quantities of oxygen are used in the formation of greater amounts of urea it is probable that an excessive formation of other products of combustion (so often asserted) does not take place. In this connection there are yet great blanks in our knowledge, to be filled by future, more extended observation. At all events, it follows from what has been said above, that fever-patients become relatively poorer in nitrogenous, and richer in non-nitrogenous elements (the latter in consequence of non-nitrogenous reduction of albuminous bodies after the separation of urea).

While, in general, the conditions for the escape of water through the kidneys is less favorable in fever than in the normal state, the amount of water evaporated is increased, and thus there is, as a rule, a relatively larger part of the ingested water excreted by evaporation. The influence of a possible new-formation of water as an ultimate product of oxidation is not to be estimated at the present time ; when the supply of water is greater some of it may be retained. The changes of the body-weight in fever are to a great extent dependent upon these changing conditions of supply and excretion of water ; the gaseous exhalations and inhalations are of much less importance. Accordingly, the question, what results from the above explained conditions of febrile metamorphosis can be made use of for appreciating the regulation of heat in fever, is answered variously by different authors. While some, on the strength of the knowledge of increase of the products of oxidation by means of which they explain the rise in body-heat, and proclaim the increase in heat-production to be the essence of fever ; others ask whether this increase is a sufficient explanation, and whether there are not other factors to be taken into consideration. Nay, some doubts even begin to be occasionally uttered as to whether increase of body-heat is to be made an absolute *sine qua non* for the conception of fever, or whether it would not be better to be content with demonstrating increased tissue-metamorphosis. Aside from this, there is at the present a complete unanimity on the proposition that INCREASE OF BODY-HEAT must be considered as the PATHOGNOMONIC SIGN OF FEVER, in so far as it depends upon an internal and special morbid state ; while those elevations of temperature which are caused only by insufficiency of the means of removing the heat produced, and which quickly pass away after renewed activity of these means (as during a stay in an excessively warm and moist medium, in a vapor-bath, after extreme muscular exertions), are not to be looked upon as febrile. By no means are we to consider elevation of temperature and fever as identical, and if, therefore, we regard the causes of the pathologically altered and especially of the heightened temperature, then we shall not have attempted to give an explanation of fever, but only of its most important symptom.

Fever is a group of symptoms which, in fully-developed cases, are as a rule, but not necessarily, found united ; for circumstances may arise which shall make the presence of one or another symptom impossible. Accordingly the setting up of our present conception of fever is to a certain extent arbitrary, though in the strongest manner justified by experience, and exceedingly practical. Elevation of the temperature of the body is the most important of the febrile symptoms, partly because it is easy to recognize, and allows the determination of the non-febrile state to be made with great certainty, partly because it undoubtedly influences to a greater or less extent the manifestation of several other symptoms of fever, such as, for example, those of the pulse, respiration, nervous phenomena, etc. The idea usually conveyed by the word "fever" is not comprehensive enough to include all the modifications of temperature occurring in patients, especially fever-patients ; we exclude from the class of fevers those conditions in which the temperature is normal and sub-normal, although many of them present a certain resemblance to the states characterized by elevation of body-heat. It is certainly not absolutely right to allow ourselves to be guided by the above-mentioned practical considerations ; but it impairs the general intelligibility of the subject if we are willing to include under the head of fever such states as collapse, large remission-periods, and a number of light cases of disease which usually run their course with increase of body-heat. It may be once more asserted that the symptom-group of fever appears united, as a rule. In this connection compare remarks by SENATOR (*Virch. Arch.*, XLV., p. 351 ; *Fieberhft. Proc.,* p. 170), and NAUNYN (*Arch. f. exper. Pathol.*, I., p. 181).

The RISE OF TEMPERATURE OF THE WHOLE BODY, which is the characteristic factor of the true febrile state, may occur :

1. By RETENTION OF HEAT BECAUSE OF INSUFFICIENT SEPARATION. A lessened giving off of heat may depend upon several conditions, but it can hardly be assumed that such conditions persist throughout the course of a prolonged febrile state ; that elevations of body-heat lasting weeks and months can thus be caused. It is a matter of every-day experience that the covering of fever-patients is more heated than that of healthy persons—consequently an outward flow of heat must occur, as usual. On the contrary, it is to be borne in mind that on the one hand a temporary retention of heat does take place and that an attack of fever may be caused, or one already present may be aggravated by it, as happens, for example, in the chill of fever ; and, on the other hand, that a continued febrile state is influenced in a special manner by such temporary retention.

According to TRAUBE (*Gesam. Abhl.*, II., p. 637), in consequence of the irritating influence of fever-producing causes upon the vaso-motor system the muscular coat of the small and smallest arteries contract strongly. The narrowing thus produced must have two consequences. The amount of blood received in a given time by capillaries from the aortic system must be diminished, and at the same time the blood-pressure within them must also fall. From the former factor there results a diminution in the amount of O transported to the tissues, and, besides, a moderate cooling of the blood by conduction and radiation at the periphery ; from the second factor there must follow a lessened separation of liquor sanguinis, that is to say, of the fluid which carries to all the tissues the necessary elements of life, and to secreting apparatuses the materials for se- and-excretion. The diminished flow of water to the superficial layers of the skin and to the pulmonary mucous membrane, necessarily leads to reduction of the evaporation from both surfaces, thus forming a second cause for slight cooling of the body. The hypothesis above cited explains, according to T., the diminution of the turgor of the skin and subcutaneous connective tissue, as well as the difference in the temperature of peripheral parts of the body and of the blood, and the sudden increase of body-heat during a chill, the tendency to dryness of the tongue, loss of appetite, and feebleness of digestive power, the composition and quantity of the urine, the stupor and muscular weakness of those sick with fever : all these are best explained by the contraction of the small arteries of the affected parts ; and the sweat of fever, the critical fall of temperature by relaxation of this tetanus. Two possible causes may exist to cause the contraction of the small arteries. The fever-producing cause somehow acts in a paralyzing way upon the heart, and thus produces, by diminishing the flow of blood in the arterial sys-

tem, a contraction of all (those necessary to a state of chill) the superficial arteries ; or, by irritation of the vaso-motor system it produces a contraction of the small and smallest arteries. In opposition to the first view, is the difference in color which is shown by a man in a chill and one in syncope, and also, more especially, the degree of tension which the radial arteries show in the period of chill ; the second assumption is the only one which is sufficient to account for the phenomena referred to.

SENATOR also (*Virch. Arch.*, XLV., p. 405) considers the retention of heat to be a process of much importance in fever. " It must be assumed that during the continued increased production of heat caused by greater consumption of albumen, there occur from time to time a moderation of the loss of heat, and that by the conjoint action of both causes an equilibrium of body-heat during large periods of time is produced, whereby a certain average is maintained." The limitation of loss of heat cannot be sought for in any other state than that of contraction of the contractile elements of the skin, especially of the small and smallest arteries, such as finds its highest expression in the chill-period ; but which may occur independently of this, even without the least rigor, and especially without any sensation of a changed condition of the skin. For the reflex phenomena presuppose a certain strength of irritation and a certain irritability, which need not always be present, or present to the same degree. How often the proper fever-heat is interrupted by such a process of contraction in the skin, whether this takes place with or without a certain regularity, and whether, possibly, the fluctuations of temperature are not dependent upon it, and, lastly, whether the process of contraction takes place equally and simultaneously in the various blood-circuits of the skin, are questions which must be resolved in the future. Both of the processes brought forward to explain the febrile temperature, increased combustion of albumen, and a periodical retention of heat, do not necessarily stand in a causal relation to each other, but go on simultaneously, and, in a certain sense, independently of one another, as results of one and the same, or of various causes, the peculiar fever-agent. The contraction of arteries is not, or is not only and not always the result of rapid increase in heat-production, and of the great difference in the temperature of internal and external parts thereby produced, but is the consequence of an irritation of vaso-motor nerves occurring without as well as with this (TRAUBE).

2. It may well be supposed that, if anywhere in the body, A LOCALITY PRODUCES INCREASED AMOUNTS OF HEAT, the SUPERFLUOUS HEAT will be DISTRIBUTED TO THE REST OF THE BODY by means of the circulation, and that the temperature of the whole body will thereby be raised. Such foci, inflammatory or merely hyperæmic, are, however, only of limited extent, and bear no proportion to the mass of the body ; and they by no means produce so much heat that the normal modes of elimination (sufficient for the relief of the largest physiological production) cannot suffice for its dispersion. It is also much to be expected that when the body is ill and the outflow of heat is insufficient, something contributes, more or less, to the increase of the extra body-heat thus produced. Furthermore, against attributing the entire fever-heat to the operation of local processes, we have the facts that in the most intense fever, *e.g.*, that of infectious diseases, the fever begins to subside upon the appearance of local lesions, while in the cases in which it goes hand in hand with the latter there is observed on the average only a moderate temperature. (*Vide* p. 273–4.)

3. Elevation of the temperature of the whole body may occur IN CONSEQUENCE OF A GENERAL INCREASE OF NORMAL PRODUCTION OF HEAT, and it is such an one as can be indicated by increase in the products of combustion. On the one hand, this can only in part be the result of increase of temperature by other causes, inasmuch as the processes of decomposition in this way demonstrably go on with abnormal rapidity ; and, on the other hand, it is evident that direct observation in fever-patients with reference to this point has afforded various, and, at least for the present, partly contradictory results, such as, that the degree of increase of products of decomposition does not by any means always fully correspond to the degree of

increase of body-heat. It is, consequently, but little probable that increased production of heat is the ONLY cause of the condition of the body-heat in fever. Apart from the fact that the normal outflow of heat suffices, at least for small increases of heat, to prevent an increase in the temperature of the body, the amount of diminution of the body-weight in fever hardly corresponds with the assumption of a destruction of bodily substance proportionate to the variations of temperature.

We are taught by the observation of febrile diseases that the products of combustion in fever, hand in hand with the increase of body-heat, are excreted in greater quantities. As regards the nitrogenous substances in particular, this influence of increased temperature is made evident by the following experiments.

BARTELS (*Greifsw. med. Beitr.*, III., p. 45) found that a sufficiently prolonged stay in a space filled with heated watery vapor produced a fever-like state; that is to say, an elevation of the body-heat, acceleration of the pulse and respiration, with increase of tissue-metamorphosis, and diminution of the weight of the body. Before the first bath (three being taken within three successive days) the subject of the experiment excreted a mean of 21.968 grm. of urea, or 0.4316 grm. to each kilo. of body-weight; under the influence of the bath a mean of 25.776 grm., or 0.5 grm. *per* kilo. of body-weight—an increase of 16 %. In the second period of twenty-four hours after the last vapor-bath the daily excretion of urea rose to 0.6916 grm. *per* kilo., against 0.3897 grm. the day before; exceeding this consequently by 77 %, and the average daily amount before the beginning of the experiment by 60 %, although the febrile action causing increased metamorphosis had previously ceased. In the ensuing three days the amount excreted was on the average 24.5 grm *per diem*, or 0.4833 grm. urea *per* kilo of body-weight; only 3 % less than during the operation of the baths. B. explains this peculiarity by a retention of urea during the baths. Its causes lie in diminution of the blood-pressure in the vessels of the kidneys owing to the enormous accumulation of blood in the skin during the period of stay in the vapor, and during the consequent prolonged (many hours) sweat, and to the considerable loss of water by the sweating, the period between two baths was not sufficient to allow a full correction of the impaired excretory power of the kidneys by absorption of water. In consequence the amount of urine passed in twenty-four hours diminished from day to day, and with it the daily amount of urea, although, owing to the artificially produced paroxysms of fever, urea was doubtless formed in larger quantity than usual. It was only after the lapse of a certain time after the last bath and perspiration that this disturbance was corrected by an increased excretion of urine and urea: hence the extremely large (greater than the proportion in health and during the vapor baths) excretion in the second day after the last bath. It must be borne in mind, however, that it is possible that a certain amount of urea, the ultimate product of the burning of albumen, may be carried away with the abundant perspiration, and that probably the increase of tissue-metamorphosis caused by the artificial increase of temperature is even greater than what is shown by direct observation.

NAUNYN (*Arch. f. Anat.*, etc., 1870, p. 159) made a similar experiment on a dog. By regular feeding he brought the animal up to a certain weight and kept it in equilibrium of nutrition, so that with a regular amount of urine the excretion of urea was quite uniform. He then increased the animal's body-heat to 42.5 C. for three hours, by placing it in a vapor-bath at 35 C.; the temperature of the body returning to the normal in the course of one hour afterward. In consequence of this artificially produced retention of heat, there resulted a very marked (even to almost one-half) increase of urea.

According to SENATOR (*Fieberhft. Process.*, p. 175), it must not be concluded from these experiments that with increase of body-heat the processes of combustion continue to become more active. "The organism," he says, "is not an oven, but, if such a comparison can be made, a machine, which works regularly only under certain exact conditions, and possesses, besides, the power of bearing without injury modifications of these conditions within somewhat restricted limits, and of correcting disorders. Among these conditions is a fixed temperature; an increase or decrease of this does not simply produce an increse or reduction of tissue-metamorphosis, but causes disorders, and produces morbid processes." Increase of body-heat produces

not simply quantitative, but also qualitative variations in metamorphosis, which at the present time are not fully understood.

The question is now to be considered, whether the increased consumption of fever causes the increased metamorphosis, or whether, on the contrary, the fever is produced by this increased tissue-change. Both are imaginable. Even *a priori* it is probable that the febrile increase of body-heat is attended by increased combustion of the tissues of the body. This can, however, be demonstrated experimentally in a satisfactory way.

NAUNYN (*Berl. kl. Wochen.*, 1869, No. 4) allowed a dog, which had been brought to a state of equipoised nutrition, to fast for two days; and observed that in this period with a temperature of 38°–38.5° C. it excreted 0.28 grm. of urea *per* hour. The animal was then made to re-acquire exactly its original weight, and was again made to fast for two days, previous to which time filtered putrid muscular juice had been injected subcutaneously, so that it was rendered feverish. In this condition the dog separated 0.42 grm. of urea *per* hour; and at the same time the amount of urine (equal amount of drink) was decidedly increased, once from 180 C. cent. to 280 C. cent. Several other experiments gave similar results.

Under certain conditions, however, the increased combustion of the tissues may itself become a cause of more, or of longer-continued increase of body-heat. If we assume that a given rise in temperature (produced, for example, by retention of heat) has taken place in the organism in a certain time, there may be in this, under the admission of a disorder of the normal attempt at equalization between the production of heat and its giving off, a cause of a lasting elevation, until this disorder shall have been remedied, and the surplus heat shall have been removed by increased giving off.

NAUNYN (*Arch. f. Anat.*, *etc.*, 1870, p. 159) produced fever in dogs by means of subcutaneous injections of muscular ichor. Immediately after the injections and before any rise of temperature, the excretion of urea appeared decidedly and uniformly increased, and remained so, as was to have been expected, during the remainder of the fever. If such an increased excretion were the consequence of elevation of temperature, it would not have made its appearance first; its early occurrence destroys (at least in the kind of fever referred to) the argument that increased consumption of tissues at the beginning of a febrile disease may precede the increase of body-heat, and that the fever-producing agent may directly cause increased tissue-metamorphosis, or a "latent fever." It is possible that in these cases the late-appearing fever may be only the result of retention of heat caused by increased metamorphosis.

Naturally, this interesting experiment by no means excludes the possibility that the increased consumption of bodily substance, which occurs later during the height of the fever, is not in greater or lesser degree only the result of the increased body-heat which is present. This points to the necessity of discussing the question, what is the proper relation between METAMORPHOSIS and INCREASE OF TEMPERATURE in fever.

There are two conflicting opinions on this point. The majority of observers conclude at once from the increased excretion of products of metamorphosis during the febrile state, to an increased production of the same during the same period, and, since with increase in the processes of combustion there must be more heat set free, to an increased production of heat. According to the other opinion, such a conclusion is by no means allowable. The various excretions of the body are not given off in an uniform manner in fever; the excretion of urea is increased in a different way from the insensible exhalations, etc. Of this there are two explana-

tions: either all the products of decomposition do not increase in the same ratio, some of them more, others less or not at all, or excretion does not exactly correspond to production, a part of the excretory substance is retained for a time, while another is expelled in a relatively quicker way. In the latter case the facilities of the febrile body for the excretion of products of decomposition must be different from those operating in the normal state, in which, generally speaking, there exists an equilibrium between production and excretion, for the body usually has the power, within certain limits, of keeping the products of decomposition at a constant quantity. If this, however, actually occurs in fever, no conclusion can be drawn from the state of the excretions alone to the amount of production in the body; at least, without simultaneous consideration of those alterations which affect the existing and considerable accumulation of products of metamorphosis.

According to SENATOR (*Fieberhft. Process*, p. 65), who has advanced the latter hypothesis, it had been previously overlooked that the body may under various conditions, according to changing amounts of excretions, become poorer or richer in substances, and that without increase or decrease of metamorphosis; and that increased excretion may very well coincide with decreased production, and *vice versâ*. Furthermore, there may, at one and the same time, occur increased excretion of substances and surplus of them in the body, even without increased production, if previously there have been abnormally small excretion or abnormal retention of substances. From this it follows that it is indispensable to investigate not merely the excretions, but, at the same time, the accumulation of products of decomposition from the beginning of the morbid action (or of the fever) until its complete cessation, or to the restoration of normal conditions, if we would have a clear insight into the relations between tissue-metamorphosis and fever.   Taking into consideration these conditions and the results which he obtained in his experiments upon purulent fever in dogs, S. forms the theory (explained at p. 663), the fundamental thought of which is that during the fever important variations of temperature, both above and below the normal, may take place.   (There is nothing strange in S.'s opinion, if we reflect that similar variations take place in the healthy state under the influence of the change from the state of digestion to that of fasting, or are caused by work and rest, and, especially, if we keep in mind the greatly increased variability of body-heat (as compared with the normal state) under obvious and various losses of heat, and its great mobility under external influences.)   Continuing his researches on tissue-metamorphosis in fever, S. (l. e., p. 88) formulates the law that in so far as conclusions can be drawn from the products of decomposition to the processes of metamorphosis, it may be stated that the intensity of these processes diminishes more and more in the course of fever, whereas a corresponding diminution in animal heat is not demonstrable, and that in fever, heat must be developed also from other processes than those which serve to produce carbonic acid and urea.   S. refers to the use of the tension-force stored up in the organism for exercise, as well as to unknown processes connected with the formation of water without oxidation (by synthesis and dehydration).   AT ALL EVENTS, IT HAS NOT AS YET BEEN POSSIBLE TO DEMONSTRATE AN EXACT RELATION BETWEEN ANIMAL HEAT AND TISSUE-METAMORPHOSIS.

It has been supposed that the question whether the production of heat was increased in fever, if so to what degree, or whether a retention of heat was the sole cause of febrile temperature, could be resolved by the calorimetric measurement of the amount of heat given off outwardly.   If this be increased, regularly so, and in a manner free from possible errors, then more heat must have been produced.   In this connection the following observations are noteworthy.

LIEBERMEISTER (*Aus der med. Klin. zu Basel*, 1868) finds that in baths of 20° to almost 36° C. the loss of heat occurring from fever-patients is greater than that from healthy persons.   For example, a patient weighing only 39 kilos. loses in a bath at 23° C. more heat than a healthy individual, weighing 62 kilos., in a bath of 22.5° C. ;

and the same patient, weighing 38 kilos., loses in a bath at 34.3° C. more heat than a healthy person, weighing 55 kilos., in a bath at 33.9° C. In this way that which, according to L., might have been *a priori* asserted (l. e., p. 126) is completely verified by calorimetric experiments. The conditions of production of heat are similar, according to L. In a warm bath the heat-production of a healthy person approximates the normal average production; in a bath at 33.9 C. it is a little greater, in one at 35.8° C. a little less. The fever-patient, on the contrary, exhibits in a bath at 34.3° C. or 34.5 C. a production of heat decidedly greater than the normal average, amounting to about one and a half times as much. It thus appears that fever-patients, even when placed in conditions as near to the normal state as possible, produce much more heat than healthy persons. Therefore, according to L., a direct proof is obtained (at least in the case of the warm bath) that *ceteris paribus* more heat is produced in the febrile state than in health (l. c., p. 128). During severe chills, with simultaneous diminution of loss of heat through external parts by contraction of bloodvessels and dryness of the skin, the production of heat may be increased three-fold, and an exact measurement shows that a fever-patient, having a temperature of more than 40 C., usually produces 20-25 per cent. more heat than a healthy person whose body-heat is 37 C. (*Volkmann's Samml. klin. Vorträge*, No. 19.) According to L., the production of CO_2 is increased in the same proportion during the chill as well as during the height of the fever. LEYDEN remarks with respect to LIEBERMEISTER'S method (according to which the patient is immersed in the bath and the exhalation of heat is measured in the water), that it must not be overlooked that the conditions of exhalation of heat in fever are much altered if the body is placed in water; and that then evaporation through the skin, which is such an important source of variations in exhalation of heat, is entirely wanting.

The method employed by HATTWICH in working out the elements of the thesis which he wrote under the guidance of NAUNYN, much resembles LIEBERMEISTER'S procedure. H. found that the loss of heat was much increased, relatively to the normal, in every stage of fever. This is opposed to the view that a diminution of the loss of heat is the cause of the febrile rise of temperature.

LEYDEN (*D. Arch. f. k. Med.*, V., p. 273) laid the leg of the person to be observed, still covered with the bed-clothes, in his calorimeter after its water had been brought to the temperature of the room. The leg lay therein under wholly normal conditions; perspiration was in no wise diminished or increased. Each experiment lasted about two hours. The amounts obtained were then calculated for the whole body in accordance with FUNKE'S relative estimate of the leg and body (149 □ inches to 2,254). L. came to the following conclusions: the exhalation of heat is increased in fever, as well with constant as with rising (not much in the chilly stage, according to a few observations) or falling temperatures; and, consequently, there undoubtedly is increased production of heat. In the highest fever the loss of heat amounts to once and a half or twice the normal value; it is by far the greatest in the critical period, then, with a rapidly declining temperature, amounting to twice or thrice the normal value; in the epicritic stage it falls below the normal. The gross amount of loss of heat may be very different with the same temperature of the blood, and it is probable that the production of heat fluctuates in the same way. At any rate, it is only with great caution that we can infer from the amount of loss of heat to the amount of production of heat. The condition of the proper body-heat must be taken into consideration: if this rises the production is greater than the exhalation, if it diminishes the latter preponderates.

According to these authors, the loss of heat in fever is much too great to allow us to consider it solely as a consequence of the fever; it can only be the increased combustion of nitrogenous ingredients of the body, estimated by the amount of nitrogen excreted with the urine, that can compensate the relatively large losses of heat, and, besides, suffice to increase the body-heat at the same time. Therefore they (LIEBERMEISTER) conjecture or assume that there is also an increased decomposition of the non-nitrogenous ingredients, and refer the increased body-heat in fever, at least in part, to a superfluous production of heat brought about in this way.

In opposition to the conclusions drawn from the investigations above referred to, in so far as they are carried out according to the method described, what has been already expressed concerning the influence of abstraction of heat upon the healthy organism may be adduced.

According to SENATOR, even the greatest possible amount of metamorphosis and

production of heat cannot by itself produce a rise of temperature comparable to that of fever, if the giving off of heat is not at the same time limited (*Virchow's Archiv*, XLVI., p. 509). He combats, in the most positive manner, the assertion that from the increased separation of heat we must conclude to increased production by increased formation of carbonic acid. It is only the decomposition of nitrogenous bodies that is abnormally increased in fever (on the average two and a half to three-fold); whereas non-nitrogenous substances do not undergo any greater combustion than in the non-febrile state of inanition. The product of their decomposition, viz., carbonic acid, is not to be found in greater quantity in the body, which should surely be the case if, as is claimed, the production of heat is increased several fold. In such a case dyspnœa at least should appear, especially in the cold bath, by which, according to LIEBER-MEISTER, a still greater production of heat would be caused; while the fact is that the bath reduces the frequency of respiration.

SENATOR admits, as demonstrated, only a few isolated facts which LIEBER-MEISTER in particular advances as in favor of a decided increase of production of heat. Among these is the increase of body-heat during a paroxysm of intermittent fever; and it is probable that something similar occurs in sudden increase of temperature due to other causes.

LIEBERMEISTER and IMMERMANN have estimated (*Prag. Vierteljahrschr.*, LXXXV., p. 39) that during the period of chill much more heat is accumulated than a healthy person could produce in the same length of time, on the average. For example, in a patient weighing 57.5 kilos. the rectal temperature increases by 2.31° C. in thirty minutes, which is equivalent (the heat-capacity of the body being reckoned at 0.83) to an accumulation of 110.2 kilo-calories, and presupposes that every part of the body has become as much warmer as the rectum has. However, since a healthy person of the same weight produces only about 45 kilo-calories in the same length of time, it is not possible that the above accumulation of heat should be owing to a diminution of the giving off of heat, or at any rate not exclusively to it, but there must have occurred an increased production of heat. L. reckons this production as at least thrice the normal amount, since some quantities of heat which we cannot as yet estimate must have been lost from the skin and lungs during the time of observation. Now it is certainly questionable, whether the temperature of the peripheral parts has increased by 2.31° C. during the thirty minutes, and, further, whether the amount of normal production or the heat-capacity has truly increased; the increase of the amount of heat invariably remains so large that S. willingly allows that the above observations demonstrate an increased production of heat, at least in the chill-period of intermittent fever. All other arguments he does not consider convincing. (*Virchow's Arch.*, XLV., p. 384.)

From more recent researches on dogs S. draws the following conclusions. In the waking state under ordinary quiet conditions, the influence of digestion being excluded (S. had already found (*Virch. Archiv*, XLV., p. 378) in this connection that in favorable cases the amount of heat produced in the fasting state was to that produced in over-feeding as 100 is to 137), the production and giving off of heat fluctuate within tolerably narrow limits. During prolonged fasting the production of heat and the excretion of CO_2 slowly decrease. During digestion both slowly increase, although the increase of heat-production is greater than that of excretion of CO_2. During refrigeration of the surface, by means of which the loss of heat is rendered abnormally great, the production of heat is demonstrably not increased, although, on the contrary, the separation of CO_2 is decidedly greater; this latter may also increase without the intervention of mechanical labor. In the early stage (one-half to two hours) of a febrile condition artificially produced by the subcutaneous injection of pus or of purulent expectoration, neither the giving off of heat nor that of CO_2 is increased in a noteworthy degree; at the height of such a fever (with a rectal temperature of 40 –41° C.) the separation of heat and CO_2 is occasionally slightly increased, though often comparatively very little above the normal. There is no proportion between the changes in both heat and CO_2. The increased excretion of CO_2, in fever when present, always falls short of the invariable increase of excretion of urea. If we calculate, from the amounts of urea and CO_2 which are excreted, the quantity of decomposed albumen and fat, we find that during a day of fever (under favorable circumstances) even less fat is burned than during a day of fasting. (*Med. Centrlbl.*, 1871, No. 47 et 48.)

A mode of estimating the production of heat which is more certain than the calorimetric method, consists in the comparison of the metamorphosis of tissue and the loss of weight of a body at one time in a febrile, and at

another time in a non-febrile condition—such as hunger. It is true that it is difficult to make such experiments upon one and the same man, yet it is possible, by the comparison of the average losses of hungry non-feverish men with those of feverish individuals, to learn that in both the loss of weight is about in equal proportions, though perhaps a little greater in the former; and we may therefore conclude that for the production of febrile heat no more body-constituents are consumed than under usual conditions.

SENATOR (*Virchow's Arch.*, XLV., p. 388) attempted to show directly that the production of heat in fever cannot be much increased. He fed dogs until they were in equilibrium of nitrogen receipt and loss, allowed them to fast for two days, and each day measured their weight and their excretion of urea. After they had recovered from this disturbance and regained their original weight he made them feverish by means of hypodermic injections of pus, and carried out measurements as before; comparing the variations in the exertion of urea and those of body-weight in the periods of hunger and of fever. Any difference observed under these circumstances must be the result of the febrile process alone. There were noted first an increase in the amount of urea exerted, and also a small and relatively smaller increase of consumption. This smaller increase of tissue-consumption in fever as compared with what occurs in the fasting state, S., judging by results obtained by himself, considers as quite compensated by the increased excretion of the products of combustion of albumen, by the increased loss of water; while the non-nitrogenous substances are not, according to him, liable to greater combustion than in the non-febrile state of inanition.

Consequently it can only be stated in a general way that the production of heat in fever is on the whole increased. Opinions differ as to the amount of increase, and it is presumably only moderate. The correctness of this supposition seems to be justified by the small, even to a certain extent doubtful increase of the consumption in fever as compared with that in the fasting state. Especially is it doubtful whether the non-nitrogenous substances take much part in this increase; it is most probable that the increased excretion of CO_2 observed under special conditions may be explained by something else besides its simultaneously increased formation. The increased excretion of nitrogen in fever only indicates a greater combustion of albumen, which, compared with the fat, of which according to rule much larger quantities are decomposed, can cause but a small increase of heat. It is not possible to decide whether this increase is primary or secondary, produced only by the heightened temperature of the blood.

A most important tissue as regards the amount of decomposition of albumen is the MUSCULAR tissue. Clinical observations show that in the majority of cases fever is accompanied by strongly-marked muscular weakness throughout the body, and not rarely also by painful sensations in the muscles (as in relapsing fever). Patients convalescing from fever remain a long time unfit for severe muscular action, and often this muscular weakness is disproportionate to the general exhaustion. We owe to anatomical investigation the demonstration of very important alterations in the muscles in fever, and in morbid processes which affect the nutrition of the tissue in a similar manner (inanition, acute anæmia, poisoning); and by chemical studies we have learned that there occurs in fever an increased excretion of creatinin and alkaline salts with the urine (SALKOWSKI, *Virch. Arch.*, LIII., p. 209), derived in all probability from the muscular tissue, which is normally very rich in these substances. Besides, direct chemical analysis is in favor of the view that muscles participate in the febrile process. According to MANASSEÏN (*Virch. Arch.*, LVI., p. 220), the maximum amount of alcoholic and watery extractive matters to be found in the muscles of feverish animals is less than the minimum of those in the muscles of animals free from fever; and, also, the amount of alcoholic extractives in the muscle of feverish animals is relatively increased, compared with the watery extractives (lactic acid? creatinin?); lastly, the proportion of nitrogen is increased in the alcoholic extract·

ives, and is not changed in the watery extractives. If the facts thus directly indi-
cate an influence of fever on muscle, such an influence is made highly probable by
a consideration of the mass and significance of muscles. Muscles constitute fully
one-half of the weight of the body; one-third of the blood not contained in the
heart and bloodvessels is in the muscular tissue; circulation and metamorphosis are
much more active in them than in many other parts of the body. It is thus easy to
understand why interruption of muscular activity (by curare, compression of the
aorta) produces a marked diminution of body-heat, and that direct measurement
has shown that, as in feverish animals, the temperature of the muscles exceeds that
of the blood in the left side of the heart, whereas the contrary condition exists in
health (HEIDENHAIN, *Arch. f. d. ges. Phys.*, III., p. 562).—Consult MANASSEIN, l. c.

R̈IHRIG and ZUNTZ (*Arch. f. d. ges. Phys.*, IV., p. 80) also insist upon the great
importance of metamorphosis in muscles for the regulation of heat; they think it
probable that the regulation of heat is in the first place controlled by constant
weak reflex excitations of the motor nerves, which vary with the differences of tem-
perature in the animal body and its surroundings. They consequently reject the
current opinion (based on the fact that body-heat is greatest in the abdominal cavity)
that the true source of animal heat is to be sought in this cavity. Especially should
we not draw too hasty conclusions from the fact that the blood of the hepatic veins
is so very warm. Whereas the heated blood issued from the muscles becomes mingled
in the peripheral organs generally with the much cooled blood of the cutaneous ves-
sels, the blood of the unstriped muscles and of the glands of the intestinal tract is
collected without cooling in the least by the branches of the portal vein. This
already heated blood next passes through the liver—an organ so completely pro-
tected against refrigeration; and thus naturally the least increase of heat produced
by processes of oxidation in the glands suffices to elevate the blood of the hepatic
veins and the liver itself to the highest possible degree of temperature.

4. In some few cases, especially those in which the question of the origin
of hyperpyretic temperatures presents itself, an increased production of
heat may occur as the result of processes more or less foreign to healthy
life, and which give rise to so much heat that the channels by means of
which heat is lost are unable to equalize the temperature; and this is more
especially the case if those channels be in an abnormal condition. Thus
in conditions of long-continued cramps and muscular contractions, in fer-
mentative processes, as well as perhaps in the febrile state produced by the
transfusion of the blood of fever, or the introduction of products of inflam-
mation or of decomposition of tissues into the organism, in abnormal
activity of the vaso-motor nerves, or particularly paralysis of one of the
central organs which moderate the body-heat.

CONTINUOUS MUSCULAR CONTRACTIONS of long duration, as for example,
in severe attacks of epilepsy and tetanus, as well as extreme muscular
exertion in general, may, especially in irritable and sensitive persons, con-
valescents, and others, decidedly increase the heat of the body. As a rule,
this disorder is corrected in a very short time, as soon as the cause ceases to
act (when, for example, the tonic contraction is over), because the channels
of escape for heat are normal and suffice for any but an excessive produc-
tion. With an abundant escape of heat no rise of temperature may show
itself; at least we often enough witness severe and prolonged muscular
contractions produce no increase of body-heat, or only a slight and tem-
porary increase of it. There is sometimes a moderate persistent fever in
diseases characterized by tonic muscular contractions, although it is not to
be assumed that these are the direct cause of the increased temperature.
If death occurs during severe tonic spasms, or with a high temperature
shortly after their cessation, then death is not brought about so much by
the stagnation of the superabundant heat produced in peripheral parts (the
muscles), as by a paralysis of certain parts of the central nervous system,
which exert a most important influence upon the animal heat (*vide infra*).

GÜNTZ (*Inaug. Diss.*, Leipzig, 1862; *Allg. Ztschr. f. Psych.*, XXV., p. 165), after experiments upon animals and man, reaches the following conclusions respecting the conditions of the temperature in the tonic spasms of tetanus. A single attack of spasm may occur without any change appreciable to the thermometer: the only consequence is a lowering of temperature without subsequent rise. After this fall, the mercury remains for a while at the same level, then rises either not quite up to its previous height or quite up to it. After the primary fall there may occur an immediate rise in a variety of ways. This re-ascent of temperature takes place in fully one-third of the cases (37) even in the first minute, more often in the third minute or later. The least amount of variation of temperature coincides with the least degree of spasm, and the most considerable rise of temperature with the most severe spasm. It is impossible to say upon what depends the regular fall of temperature which takes place just before or during the spasms.

LEYDEN has also attempted to investigate, by means of experiments on rabbits and dogs, what share the abnormally increased muscular action had in the unusually great increase of temperature observed in fatal tetanus (WUNDERLICH cited at p. 625). The animals were tetanized to exhaustion by means of broken electrical currents; the electrodes being inserted under the skin of the back. There was found a rise of only 1 C. in rabbits, of 5 C. in dogs (*Virch. Arch.*, XXVI., p. 538).

BILLROTH and FICK (*Vjschr. d. Natrfrch. Ges. zu Zürich*, 1863, VIII., p. 427) experimented in the same way. They observed in dogs a rise of fully 5 C. They also determined the existence of a fall of temperature introducing the attack of spasm, in the rectum; a thermometer introduced between the muscles of the posterior part of the thigh showed, during the intervals of rest, a greater fall of temperature than that indicated in the rectum, and showed a quicker rise during the attacks. In general, the maximum of temperature appears later in the rectum than in the muscle, if the tetanus be interrupted: this being explained by the fact that at the close of the tetanus the muscles are warmer than the other tissues, and that then the rectal temperature rises by equalization of the body-heat. In the same manner a partial explanation of the *post mortem* temperature may be made. BILLROTH (*Arch. f. klin. Chir.*, XIII., p. 614) made the supplementary observation, that the rise observed in the thermometer during attacks of spasm (the instrument being in the muscles) is not caused or modified by compression of the mercurial bulb, but expresses a true increase of temperature. He furthermore observed that a tetanus localized in the right leg was sufficient to raise the temperature of its muscles to a point higher than that of the rectum; the equilibrium between the two temperatures being reached after about one hour.

WUNDERLICH (*Arch. d. Heilk.*, 1864, V., p. 223) thinks LEYDEN'S idea, that in tetanus the want of the discharge of muscular action into mechanical labor (if the muscles are mutually in equilibrium, there is, so to speak, no motion produced) is capable of increasing body-heat (according to BÉCLARD), worthy of consideration. The same factor may also play a part in the rise of temperature observed in fettered animals (compare BILLROTH, l. e., XIII., p. 611).

To the category of fevers presumably produced by fermentative processes, belong all those which ensue after injuries of all kinds. There is a large number of wounds, some of them severe, in which no fever shows itself. Consequently, fever is not an essential accompaniment of wounds as such, but is always an accidental affection. The period during which a wounded person may develop fever varies from the time of the reception of the injury to the healing of the wound. It is, however, the rule that, in those cases in which fever makes its appearance, it begins on the second day and continues until the seventh. The duration of traumatic fever is even more variable than the time of its first appearance. If a subject of operation is free from fever at the expiration of the fourth day, he will probably remain without fever.

If the temperature of operated patients be carefully taken both before and after the operation, it will be found that, as a rule, the body-heat first sinks, though seldom under the normal, and very soon reascends. Continuous observations reveal three principal types, as follows: 1. The variations of temperature remain within the maximum of the normal range (assuming

this to be 38° C.). 2. The temperature slowly rises above 38° C. 3. It suddenly rises, and usually much, even to as much as 40° C., in a few hours. At times there are intercurrent falls of temperature, which are usually followed by renewed elevations. It is absolutely established that the mode of injury and its immediate consequences, as far as effects upon the tissues are concerned, do not by themselves constitute factors capable of explaining the states of the temperature referred to above.

BILLROTH (*Arch. f. klin. Chirurg.*, 1872, XIII., p. 579), whom the author follows in stating these phenomena, refers to the following conditions as capable of modifying the body-heat immediately after operations.

a. LOSS OF BLOOD. Large losses of blood, and naturally those occurring spontaneously as well as those produced by bloodletting, are followed, in the sick as in the well, by a rapid falling of the temperature, which, if death or a marked improvement in the disease does not take place, is soon corrected. The effect of bloodletting is a very transitory one. According to TRAUBE, even the radial artery may, after a copious bloodletting, re-assume its former degree of tension in a few hours, and at the end of the same length of time the thermometer will indicate a higher temperature than before the operation. The observations of ZIMMERMANN (*Ztg. d. Ver. f. Heilk.*, 1855, No. 27) on man, and those of BERGMANN (*Petersb. Ztschr.*, XV., p. 89) on animals, as well as those of FRESE and KETTLER (*Diss. Dorpat*, 1866 et 1867; *Virch. Archiv*, XL. et XLIII.), are in agreement with the above. BERGMANN explains the secondary elevation by the augmented entrance of products of physiological metamorphosis into the vascular system, as must take place because of the lessened lateral pressure upon parenchymata. Since this elevation of temperature takes place in well persons, there is no need to assume a special irritation of the tissues as necessary to the formation of such "pyrogenic" products. In this connection compare GIETL (*Die Cholera u. s. w.* München, 1855), who supposes that "fever is chiefly produced by a certain alteration in the fluids of the tissues, brought about by certain substances." (Possibly the severe attacks of fever which appear after a diarrhœa at first not attended by fever, in children, are to be explained in the same manner as the rise of temperature after bloodletting.)

b. THE NARCOSIS OF CHLOROFORM. Under the influence of chloroform there occurs a lowering of the body-heat, presumably caused by diminution of the rapidity of metamorphosis in consequence of reduced activity of the heart-muscle. The property which chloroform has of reducing the temperature of the body was known through DUMERIL and DEMARQUAY, in 1848. (Compare SCHEINESSON, *Arch. d. Heilk.*, 1869, X., p. 36.) The latter discovered that this fall of temperature took place as well under conditions which rendered increased loss of heat though the respiratory organs impossible, as under such as reduced the loss of heat through the skin to a minimum. This points to lessened production of heat.

c. THE PAIN OF WOUNDS. This takes but little part in the reduction of temperature which is observed immediately after injuries. According to HEIDENHAIN (*Arch. f. d. ges. Phys.*, III., p. 508), the temperature of the internal parts of the body falls upon irritation of sensory nerves anywhere. It rises again after cessation of the irritation, sometimes rapidly, sometimes unusually slowly, so that by means of repeated irritations, each of which causes a rapid fall of temperature, a marked and lasting depression may be produced. Perhaps the section of large nerve-trunks exerts a lowering influence upon the body-heat. JORDAN and FISCHER (*Volkm. Samml. klin. Vorträge*, No. 10) observed in "shock" (which according to F. is to be considered as a reflex paralysis of the vascular nerves, particularly of the splanchnic), produced by traumatic irritation, a decided lowering of the body-heat. BILLROTH, though unable to support this view by experiments, concedes that the wounding of internal organs at least can produce such an enormous diminution of temperature as would not be produced by the concomitant loss of blood. By means of irritations continued 2–3 hours he could not with certainty produce fever.

d. PROLONGED EXPOSURE OF THE PATIENT. After operations performed in insufficiently warmed rooms there occurs a moderate degree of collapse, a proof of the insufficiency of the heat-regulating power of the organism when the loss of heat is too great. (SENATOR.)

If, through the above-named circumstances, the normal condition of temperature has been changed to an abnormal one, it is easy to understand that

a further disorder easily sets in—that the patient is feverish after a longer or shorter time.

All the remaining phenomena of traumatic fever in man are best explained by the hypothesis, that it is dependent upon inflammations set up, not by the injury itself, but by septic processes taking their start in the wound. It is most probable that the fever is caused only by spores which enter the blood through the wound, and that SEPSIS is the result of vibrionic putrefaction. To what degree these inflammations of the wound and the fever dependent thereon are developed, or whether they develop at all, depends upon the nature of the wound, the mode of dressing, the state of the atmosphere in which the patient is, the mechanical factors which favor the entrance of putrid substances into the tissues and the blood, upon the quality of the putrid substances, the intensity of their inflammation-producing (phlogogenic) and heat-producing (pyrogenic) activity, etc. Consequently, if immediately after a wound or operation the temperature suddenly rises, it is possible that an infection, direct or indirect, of the wound has occurred, or that inoculation with a pyrogenic substance has taken place. Among other means, the quick removal of the infecting inflammatory focus is necessary in order to bring the fever to an end.

The following account of the simple fever which accompanies wounds, "traumatic fever," is sufficient for clinical purposes. Traumatic fever lasts from one to seven days and more, without any tendency to cease on any particular day; it is continuous with the secondary fever (after the seventh day) in cases of severe injury, and even in cases of accidental inflammation and suppuration. The highest temperature is attained in traumatic fever on the first or second day, seldom from the third to the fifth days, very rarely later still; the temperature may rise higher in the secondary fever.

In SEPTICÆMIA, the temperature is, as a rule, very high in the beginning, and later becomes very low; though there are cases in which it is low at the commencement and never rises very high; and even in some rapidly-fatal cases it sometimes hardly exceeds the normal. Death may occur at any point of these oscillations of temperature; or it may follow a rising high temperature, or one falling far below the normal. In its course chills are exceedingly rare.

The same features characterize the PYÆMIC forms of disease, when these are superadded, so that the distinction of traumatic from purulent fever, and still more that of septicæmia from pyæmia, is only a graduated and uncertain one, because of the absence of objective statistically useful data. As a rule, the beginning of fever in the pyæmic form is distinguished by great rise of temperature during a chill, after the previous existence of a more or less marked fever, or after none at all; and yet it cannot be assumed that the more intense dangerous infection has taken place in this chill. Immediately before the chill, the temperature sometimes exhibits a short depression, sometimes an elevation, or again no change at all; during the chill it usually rises above 40° C., and often attains nearly to 42° C., and afterward it falls suddenly almost to the normal, as a rule. At this time an exceedingly variable course of temperature sets in, chiefly modified by the rapid or slow sequence of the succeeding chills, as well as by the average temperature of the remaining course of the disease. The chills, with their accompanying enormous or moderate elevations of temperature, follow each other more or less frequently. Generally they are few in number, rarely more than five or six before death; still more rarely does a patient have more than one chill in twenty-four hours; and they occur

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much more often in the daytime than at night. In the interval there is sometimes, during several days, a tolerably regularly remittent, or even a continued type of fever; though more usually there occur more or less irregular variations of temperature even down to the normal, in the vicinity of which the temperature may linger for days. Death may take place at any time during such a course of temperature, as well with a normal or nearly normal body-heat as with greatly increased temperature. The much rarer recovery, which occurs only in mild cases, makes its appearance after cessation of the chills, and with a gradual decline of body-heat. Nothing certain can be stated about the duration of pyæmic fever, because it is impossible to determine with exactitude at what time the dangerous or even fatal infection began. The patient will succumb or recover sooner or later, according to the intensity of the poison, the power of resistance he possesses, etc.

A number of observers have instituted experiments to determine the nature and the mode of origin of septicæmic and pyæmic fevers.

The oldest noteworthy investigations of BILLROTH and O. WEBER date from 1862–4; and in what follows mention will only be made of the most important contributions of still more recent date.

BILLROTH (*Arch. f. kl. Chirurg.*, XIII., p. 628) injected a small amount of filtered infusion of putrid dog's flesh in the blood, or under the skin. With relatively large amounts death soon ensued with a rapid fall of temperature; with smaller amounts there occurred a rise of temperature, usually even in the first hour, sometimes in the third or fourth hour, and this fever lasted from four to eight hours. Fresh pus injected into the blood or into the cellular tissue sometimes produced fever, sometimes did not. After injection of large amounts of water a disturbance of temperature, perfectly analogous to that set up by injection of pyrogenic fluid, may show itself; consequently the positive result of the above experiment is very uncertain. The temperature of the water used for injection is without influence, and the evacuation of a quantity of blood corresponding to the volume of water does not prevent the elevation of body-heat.

BERGMANN (*Petersb. med. Zeitschr.*, XV., p. 16) discovered, by means of numerous experiments upon pyæmic and septicæmic processes, that after the injection of putrid substances and of the tissues of inflamed parts, there occurs a sudden rise of temperature, quickly followed by a fall to the normal, if death or further local disorders does not take place. It was further shown that after the injection of large quantities of distilled water, or after transfusion of healthy blood or blood-plasma, the same oscillation of temperature may occur, though usually to a moderate extent. Therefore B. came to the conclusion "that there is only a graduated difference, not a specific one, in the effects of putrid matter, products of inflammation, or products of ordinary metamorphosis upon body-heat; that it is not merely specific inflammatory products which, circulating in the blood, act as fever-producing agents, but that the same effect may result from substances which have been produced by decomposition of tissues in the usual course of metamorphosis."

Injection of putrid substances directly into the veins shows "that immediately after the injection the temperature begins to rise, reaching a maximum between the second and third hours, and returning to the normal in three or six hours. As soon as lesions occur at the punctured spot or at a distance from it the body heat remains for a long time above the normal. In the worst cases of putrid injection, which conduce to death in twenty-four hours, the temperature at first rises in a typical way, remains elevated for a while, and often falls a good deal just before death." With injections into the subcutaneous cellular tissue the temperature-curve varies with the local inflammations which arise. In case of slight local trouble there occurs a sudden rise of temperature immediately after the injection, and then a prolonged slight fall to a certain height. Before the breaking of abscesses there is always an exacerbation. In case of a severe local lesion the fever runs a course quite parallel to it; it remains continuously at a considerable height until death, and it is only during the agony that for a shorter or longer time there is a fall.

Furthermore, B. experimented with pus and other products of inflammatory disintegration of tissues. He injected pus-serum as free as possible from corpuscles obtained by filtering pus diluted with water; and the filtration was done under so

low a temperature, and so little time (not more than an hour) was allowed to elapse between the obtaining of the pus and its insertion into the animal, that the fluid used in the experiment may be considered as unchanged. After the introduction of relatively small quantities of pus-serum in the circulation, there appeared exactly the same temperature-curve as after the injection of putrid substances. The above-described typical fever, following at once upon the injection, passed into a more or less prolonged atypical fever only when further local lesions were produced by the operation itself or by the injected substances. Subcutaneous injections of fresh or boiled pus and pus-serum exerted precisely the same influence upon the temperature as injections of putrid fluids. As an indirect consequence of the elevation of temperature produced by resorption of the injected matter, there may arise anew a fever dependent upon a local lesion. This fever keeps pace with the local trouble, increases with its spread, remains at a stand-still as long as this does not increase, and ceases upon its disappearance.

Besides, B. injected the fluid of acute inflammatory œdema and of inflammatory transudates, but only under the skin. It was first shown that there were set up rapidly extending inflammatory processes in the subcutaneous cellular tissue. The temperature increased as before ; but the peculiarities of those parts of the fever-curve which were connected with the local lesion were interesting. An exacerbation by pushes (*schubweises*) is characteristic of the fever of progressive suppuration ; and there occur in its course sometimes remissions with regular evening exacerbations, sometimes intermissions. It is otherwise in acute inflammatory œdema. In this the fever resembles that of acute septicæmia in man ; febrile paroxysms are not noticeable, but the temperature rapidly rises to a considerable height, and continues at that elevation.

B. furthermore established that the elevation of temperature observed in his experiments did not depend upon other causes than those brought to bear in the experiments, as, for example, individual variations in the physiological body-heat of the animals experimented upon, strong muscular exertions, etc. Injections of neutral substances, *e.g.*, distilled water, produced no elevation ; while, on the contrary, this did show itself after the injection of large volumes of water, and small amounts of irritating substances, *e.g.*, sulphide of ammonium, in the same manner as after injections of pyrogenic materials. This B. explains by the assumption that these substances first irritate the tissues, and that it is only the products derived from irritation of tissues which act in a pyrogenic manner. Among other things which are in favor of this explanation, there is the elevation of body-heat through increase of oxidation-processes in the organism, as produced in animals by the injection of binoxide of hydrogen (ASSMUTH. *Diss. inaug.*, Dorpat, 1864) ; and as shown after withdrawal of blood (*ride supra*). Besides, the comparison of transfusion of healthy and of feverish blood in dogs teaches that the former transfused in small quantity produces no increase of body-heat, that when used in greater quantity it sometimes give rise to a distinct fever, and that this is regularly produced by transfusion of feverish blood. Consequently feverish blood does not operate in a specific manner, but only differs in degree of activity from healthy blood. The temperature after injection of feverish blood appears just as it does after injectious of putrid fluids, and B. rightly sees in this a confirmation of his opinion that the fever-producing effect is obtained by means of natural products of tissue-metamorphosis.

Consequently, observations upon variations of temperature after diverse injections did not enable B. to determine differences in the substances injected.

BILLROTH (*Arch. f. klin. Chir.*, XIII., p. 635), as well as others, has corroborated BERGMANN'S observations.

With respect to the ORIGIN OF THE ELEVATION, BILLROTH advanced the opinion (*Arch. f. klin. Chir.*, IX., p. 118), that traumatic and inflammatory fevers arise through the absorption of pyrogenic substances, produced upon or in the wound, or from such as are deposited upon it. The intermissions of traumatic fever chiefly depend upon the intermittent taking up of the infecting body into the blood ; and he also noticed that chills were more dependent upon the absorption of purulent than upon that of ichorous matter. "Once introduced into the tissues, the poisons in question act like ferments ; it is not by an atonic infectious substance that the infected individual is made so very ill, but because the atom of poison sets up an inflammation whose products are highly toxic, and it is these which repeatedly poison the blood. . . . . The infectious substances of this category all act, in the first place, in a phlogogenic way " (p. 123).

In his most recent work (l. c., XIII.) B. does not maintain this view so absolutely, but, because of its similarity under different conditions, and because of its rapid

development and short duration, he does not connect the initial fever of experiments by infection, with an inflammation. Inflammation is not produced by injections of water, blood-serum, etc , which do set up fever. Incidentally he refers to the fact that although embolisms of the pulmonary artery produced by particles of starch and charcoal cause fever, they do not set up inflammations, as an additional proof that the former may exist without the latter.

BERGMANN (l. c., p. 44) thinks that we do not possess any positive evidence showing that there occurs a kind of fermentative change in the blood after injections of putrid substances. As far as increase of temperature is concerned, the results of injection into the veins are certain proof that the infection-fever is transitory ; when there is persistent fever there must accordingly be a constant supply of fresh infectious material to the blood, and this probably from newly-produced local disorders. In putrid intoxications there is question of a poisonous effect completely analogous to the operation of other toxic solutions injected into the blood ; death follows, or the poison is quickly eliminated, and the disorder subsides, or else there are developed lesions here and there, which may of themselves give rise to new general phenomena (among others to fever). It is only the first-observed increase of temperature which can be referred to the absorption of the poison, while the remainder of the fever-curve (by far the larger part) must be attributed to the effect of local lesions. That the first rise of temperature in case of subcutaneous injections cannot be produced by local processes, is shown besides by the quickness with which it appears (which is quite as great as when the injection is made in the veins), especially by those cases in which reaction at the point of injury is absent, and in which the temperature rises and falls according to the type characteristic of injections of putrid solutions into the blood.

According to SAPALSKI (Verh. d. Würzb. phys. med.-Ges., III., p. 142), in the operation of pus-injections there is neither a condition of simple retention of heat nor a mere combustion of the injected substances, but there is produced a long-continued increase of production of heat which must be dependent upon a special long-acting, ferment-like effect of the pus.

It has been sufficiently well established by numerous contributions, how great an influence the CENTRAL NERVOUS SYSTEM exerts upon the distribution of blood throughout the organism, and upon the temperature of its various parts. This influence is chiefly owing to the capacity which the nervous system has of producing contraction of the muscles of bloodvessels. Our knowledge of the influence of the central nervous system upon the production of heat is very much less.

LUDWIG and SPIESS discovered that the secretion of the sub-maxillary gland produced by irritation of the chorda tympani showed a temperature 1 –1.5 C. higher than that of the blood of the artery leading to the gland, and concluded that an increased production of heat takes place under the influence of nervous excitation. Besides, pathological observations show that injuries of the central nervous system are capable of causing increased production of heat. BRODIE (Med.-Chir. Trans., 1837, p. 416) found that at the end of forty-two hours after crushing of the lower part of the cervical enlargement of the spinal cord, the temperature was 43.9 C. ; BILLROTH noticed, fifty hours after crushing of the spinal cord consequent upon a fracture of the sixth cervical vertebra, 42.2° C. ; SIMON saw a man die with a temperature of 44 C. three days after contusion and apoplexy of the dorsal part of the spinal cord, with fracture of the twelfth dorsal vertebra ; NAUNYN observed, nineteen hours after fracture of the fifth and sixth cervical vertebræ and crushing of the spinal marrow, 43.6 C. in the axilla, and already fourteen hours before it had been 37.6 C.

Since the rapidity with which the rise of temperature made its appearance, and the absence of preceding signs of irritation make it unlikely that the elevation was caused by any reactive inflammation of the spinal cord, it appears certain that in man a great increase of temperature may be produced by section of this organ, especially in its lower cervical part.

The results of experimental injuries to the spinal cord in animals have given results in striking contradiction with the above clinical experience.

After total section of the spinal cord there usually occurred a more or less rapid decrease of body-heat.

TSCHESCHICHIN found, after section of the spinal cord (the more marked the higher the section was made), a diminution of temperature; and on the contrary a carefully done transverse section of the medulla oblongata, so made that it touched the posterior part of the pons Varolii, almost instantly caused increased rapidity of the heart's action, of respiration, of the blood-stream, and an elevation of temperature. These phenomena were, consequently, produced by the integrity of the spinal cord and by the increased activity of its centres, which are in a measure independent and as such more active, but which are also dependent upon the brain which moderates their actions and holds them in equipoise. T. refers to the moderating centres described by SETSCHENOW in the brain, centres whose excitation reduces reflex actions, and whose palsy increases them. (*Arch. f. Anat., Phys. u. s. w.*, 1866, p. 151; *D. Arch. f. klin. Med.*, II., p. 599.) Besides, he accidentally discovered that it was possible to retard or even to prevent for awhile, the usual rapid sinking of the temperature which follows section of the spinal cord, by carefully covering the animal.

FISCHER (*Med. Ctrlbl.*, 1869, No. 17) concludes from experiments and clinical observations that there exists in the cervical part of the spinal cord an inhibitory (or regulatory) centre for temperature, excitation of which causes a rise of temperature, and thinks that this centre must be sought for in the anterior columns of the cervical enlargement.

HEIDENHAIN (*Arch. f. d. ges. Phys.*, 1870, III., p. 578) observed that: section of the brain at the limit between the pons Varolii and the medulla oblongata may cause an increase of body-heat; injury to the posterior border of the pons and the anterior part of the medulla by a simple stab with a needle is no less effectual, while such a wound of the anterior border of the pons is without effect. The rise of temperature frequently begins immediately after the operation; occasionally this is preceded for a short time by a depression. The rise thus produced may last until death; in other cases, after a certain height has been attained, the mercury begins to fall, and in such a case a second stab may cause a renewed elevation. The increase of temperature does not take place merely in internal parts, but in the peripheral parts of the body. H. infers from this that the elevation is not due to a diminution of the giving off of heat, but to an increase of heat-production. The assumption of TSCHESCHICHIN, that the increase of temperature is consequent upon the separation of hypothetical moderating cerebral centres, does not appear tenable to him. It appears much more probable to him that this may depend upon excitation of the centres which regulate the temperature of the body, and tries to fortify this opinion by means of experiments consisting in electrical irritation of those parts of the brain, by which in the course of one or two minutes an increase of body-heat is produced.

Further investigations upon the influence of the nervous system upon body heat showed H. (l. c., p. 504), that by irritation of sensory nerves, the temperature of the arterial blood, as well as that of the internal parts of the body, is made to fall 0.2° C. in 1–1½ minutes, and that this depression does not appear if the medulla be separated from the spinal cord; while separation of the former from the pons is without effect. Immediate irritation of the medulla oblongata by electrical means or interruption of artificial respiration operates in a similar way. It follows that irritation of sensory nerves exerts an influence upon the temperature only through the medium of the medulla oblongata. At the same time, with depression of the temperature there occurs an increase in the arterial pressure, and the speed of the blood is made more rapid; and in consequence there is a greater giving off of heat from the surface of the body. The diminution of temperature must, consequently, be the greater, the cooler is the surface. In accordance with this, H. finds that in a cold bath of 14–18° C. the internal heat rapidly diminishes, and that this fall is hastened by irritation of sensory nerves. In a warm bath the temperature rises, and irritation of sensory nerves slightly retards this rise. If, consequently, all the observed phenomena can be explained by alteration in the giving off of heat from the surface, the hypothesis of an immediate influence of the nervous system upon the production of heat is not required. In feverish animals the artificially produced decrease of temperature does not at all occur, or appears but slightly—a circumstance which H. would explain by the increased temperature of the surface. The influence of nerve-irritation at once shows itself if the surface be artificially cooled.

NAUMANN had already (*Prager Viertejhseft*, 1867, XCIII., p. 133; *Arch. f. Phys.*,

V., p. 201) called attention to the fact that irritation of sensory nerves, as for example in consequence of a strong irritation of the skin, constantly produces a diminution of body-heat. This shows itself, according to him, usually after a shorter or longer period of increased temperature which is often noticed during the irritation, often begins after the cessation of the irritation, and frequently does not come to an end in half an hour.

According to HEIDENHAIN, this diminution of temperature is brought about by changes in the circulation. At first the resistance to the flow of blood increases by a wide-spread contraction of the smaller arteries, though through this the activity of the heart increases more rapidly than the resistances, thus causing greater rapidity of the blood-current. In consequence of this more rapid circulation, larger quantities of blood pass through the colder peripheral parts of the body in a given time. Thus there is brought about a more rapid partial equalization between the latter and the warmer internal parts. While the temperature of the periphery increases, and therefore the loss of heat outward becomes greater, a fall of temperature must occur in internal parts. RIEGEL (*Arch. f. d. ges. Phys.*, IV., p. 383) denies the constancy of the above phenomena, as well as the admissibility of HEIDENHAIN's explanation.

On the contrary, NAUNYN and QUINCKE (*Arch. f. Anat., Phys. u. s. w.*, 1869, pp. 174 et 521) showed that crushing of the spinal cord (usually at the level of the sixth cervical vertebra, within the slightly opened dura mater) is followed by an increase of temperature ; that this rise is so much the greater, the higher the crushing is done, and that this elevation of temperature with the greatest probability must be referred to an increase of production of heat. He explains the fact that all former observers had observed a lowering of temperature after division of the spinal cord, by the twofold effect of this operation, the one an increase of heat-production, and the other an increase of the giving off of heat, as caused by the abolition of the activity of the vaso-motor nerves in the palsied parts. These two results of division of the spinal cord operate in an antagonistic manner, so that the resultant, the body-heat, must rise or fall according to the preponderance of one or the other effect. In small animals, and under circumstances favorable to loss of heat, there is generally observed diminution of temperature ; but by modifications of external conditions by which sometimes heat-production, sometimes loss of heat is favored, it is possible to obtain either a rise or a lowering of temperature. An elevation is chiefly observed if the largest possible animals be made use of, since in them loss of heat is notably diminished.

RIEGEL (*Arch. f. d. ges. Phys.*, 1872, V.) and ROSENTHAL deny that from the rise of temperature following section of the spinal cord the conclusion of increased production of heat can be drawn ; there is only a greater loss of heat compared with what takes place in normal animals.

Consequently, it seems to be established that by the above-named injuries to the nervous system the regulation of heat in the animal organism may be so disordered, that with increase of heat-production and of loss of heat, the body is no longer capable of maintaining its normal temperature : the result of such a disturbance of equilibrium is, under favorable circumstances, a lasting rise of temperature above the normal.

It is, however, not proven that every increase of body-heat must be referred to a disorder of the central nervous system ; and still less is the nature of this disorder understood.

NAUNYN and DUBCZANSKI (*Arch. f. exp. Pathol.*, I., p. 181) have attempted to solve this question in the case of the fever produced by injection of pyrogenic substances. Those substances may be considered as fever-exciting, for the reason that they cause a primary functional disturbance of those parts of the central nervous system which regulate animal heat, or because (according to KLEBS) they contain, on the one hand, materials which possess the power of transporting oxygen, i.e., of acting as oxidizing agents, and on the other hand they are collectively in a fermentable state, and can induce fermentative processes in other parts of the body, and it is upon their occurrence that the appearance of oxidizing substances depends. Fermentation is by no means limited in extent by the amount of ferment introduced. Now, SAPALSKI observed in many experiments that the temperature did not rise after the introduction of active pyrogenic substance in rabbits, but that it, on the contrary,

diminished, and he was obliged to assume that this fall is caused by the enormously increased loss of heat in the febrile condition; it can be checked by raising the temperature which surrounds the animal, and by this means even an elevation of body-heat may be obtained. In accordance with this, N. and D. found that when a small animal was injected with pyrogenic matter, increase of its body-heat was constantly observed only if the surrounding atmosphere was at a temperature of at least 24° C. When this was less than 24° C. the results began to be variable; and the lower the temperature was, the more surely did a lowering of body-heat follow the injection; this surely occurred at a temperature of 15–16° C. In the case of dogs the influence of the external temperature is much less, and such an influence is marked only after the hair has been removed from the animal. If the loss of heat from small animals be diminished by wrapping in a thick layer of cotton-wadding, a distinct elevation of body-heat may be observed, with an external temperature which, without this precaution, would prevent the rise, or even cause a fall of body-heat. According to these experiments, it is certainly not right to attempt to explain the *modus operandi* of pyrogenic substances simply by an increase of animal heat, but rather by the assumption that the animals experimented upon are to a certain extent placed in a condition of labile (changeable) equilibrium of temperature, in all important particulars just like that in which they are put by the operation of division of the spinal cord.

It appears from these investigations that fever, especially that which is produced experimentally by sepsis, and presumably also the traumatic fever of human beings, is chiefly a vaso-motor phenomenon, produced by disturbance of function of certain parts of the central nervous system, viz., those which serve for the regulation of animal heat. It is most probable that there occurs a paralytic state of these parts, and that thus there is simultaneously produced increase of the giving off of heat and of heat-production. It is by no means necessary that the disorder of innervation of the cutaneous bloodvessels and that of those of internal organs should bear a certain and constant equal relation to each other; increased heat-production is not invariably the cause of increased loss of heat, and *vice versâ ;* the two phenomena are to a certain extent independent. That both may be consequences of vaso-motor processes, cannot be denied; as this is established, for example, by the well-known influence of division of the spinal cord upon the smaller vessels of the skin and upon cooling of the body. Whether the result of increase in both factors of regulation of heat is an increase of body-heat or not, depends only upon the fact that one or the other preponderates.

From such considerations it necessarily follows, however, that IN TRUE FEBRILE STATES OF THE HUMAN ORGANISM THERE MAY BE PRESENT A NORMAL OR EVEN SUB-NORMAL TEMPERATURE. It is true that external conditions (atmospheric temperature, covering of the skin, etc.) do not act upon men to the same degree as upon small animals, in the first place because of their larger size; hence there are smaller variations of body-heat in men, and, under certain conditions, there is always observed a marked elevation of temperature toward the fatal end of disease.

In this way some clinical facts can be easily explained. For example, the circumstance that certain mild cases of typical infectious diseases characterized by a regular course of fever, may progress with no elevation of temperature, or with a very small rise, while at the same time the absence of the normal type of body-heat as observed in health is wanting, and thus an irregularity is indicated; and, also, the occasional variously sudden and even interrupted rise and fall of the temperature under circumstances in which it, as a rule, follows a regular course; etc.

Lastly, the question has been studied, whether the impulse to increase of temperature, in traumatic fever, is given by infection of the blood, or by the irritation which is exerted by the inflammation upon the nervous system.

BREUER and CHROBAK (*Jahrb. d. G. d. Aerzte in Wien*, XIV., p. 3), with this object in view, resected all the nerves of a part of the body, and, after healing of this injury, produced severe injuries of bones and joints. The temperature rose and ran its course just as in normally innervated extremities. They, therefore, concluded that traumatic fever is independent of the nervous connection between the inflamed parts and the nervous centres. On the other hand the depression of temperature which severe injuries of the joints cause, seem to depend upon these nervous connections, since it was altogether wanting in case of preceding resection of the nerves.

As regards the very extreme terminal elevation of temperature, much higher than the usual range of fever, which sets in at the close of severe lesions, especially of the nervous system, it seems well-established that it is not to any important degree produced by abnormal muscular activity. It makes its appearance along with clonic or tonic spasms of all kinds, and even without these along with symptoms of severely disturbed and depressed cerebral functions. These facts are in favor of the existence of contrivances in the central nervous apparatus, such as have been discussed when speaking of the effects of section of the spinal cord, in disorders of which the production is increased to a degree not possible when the nervous activity is normal. Respecting the influence of loss of heat, it is remarkable that such enormous final excesses of temperature seem to show themselves more at the time of the greatest heat of summer, than in any other season. The great rise begins sometimes suddenly after a normal course of fever only a few hours before death; at other times it develops gradually in the course of a few days, as a continuation of a gradual increase of temperature; or, again, it ensues after totally irregular variations of body-heat. This symptom of approaching agony is usually accompanied by other severe symptoms, produced through the nervous system.

In addition, there is not rarely observed a short *post mortem* elevation of temperature after the cessation of the heart's action and of respiration, or even after actual death (vide pp. 624–5). This is not, however, necessarily associated with a pre-mortal rise of temperature, but may appear without this, though it would seem in a less characteristic and marked manner.

Concerning the origin of this *post mortem* increase, VALENTIN (*D. Arch. f. kl. Med.*, VI., p. 200) came to the following conclusions. The *post mortem* production of heat is a process common to all bodies, which appears in a certain gross amount only in some cases. As soon as it is noticeably larger than the simultaneous loss of heat, *post mortem* elevation of temperature makes its appearance. The same occurs when the production of heat is increased, and when the loss of heat is diminished. *Post mortem* rise of temperature is chiefly due to the persistence of the heat-producing vital processes after the cessation of cardiac contractions; increased activity of these processes, which is mainly brought about by nervous influence, causes a marked *post mortem* production of heat. The development of *post mortem* muscular rigidity, although in its occurrence a little heat is liberated (HUPPERT, *Arch. d. Heilk.*, 1867, p. 321), exerts only a subordinate influence upon the *post mortem* rise of body-heat. The decompositions which occur after death probably act as not unimportant sources of heat. Loss of heat is, under similar circumstances, much less after death than during life; and by this, without increased production, a *post mortem* rise of temperature is rendered possible.

According to HEIDENHAIN (*Arch. f. d. ges. Phys.*, III., p. 527), *post mortem* elevation of temperature is a constant phenomenon in dogs. In smaller animals whose heat-producing mass stands in an unfavorable relation to their heat-losing surface, the impaired giving off of heat makes itself apparent (as VALENTIN had already pointed out) by retarding the rapidity of refrigeration. The most important cause of this diminished radiation of heat must be sought in the cessation of the circulation of the blood. The temperature rises in the interior of a dead body for the same reason that it rises in a living body after interruption of the circulation: chemical decompositions continue while loss of heat is diminished.

5. Increase of body-heat may arise through a combination of several of the conditions which with respect especially to statements in 1 and 3, occur in so many cases. If this possibility be borne in mind, it is conceivable that the same height of febrile temperature in two cases, or at two separate times in the same case, may have a very different causation and significance. With the same degree of heat, production of heat may be much, or little, or not at all increased, in proportion to the amount of loss of heat; and for this very reason the febrile waste and the amount of febrile products of decomposition may in the one case be small, in the other large. And likewise, with various production of heat and equal body-heat, the determination of the amount of loss of heat may yield a very different result; a state of things based on facts.

According to OBERNIER (*Berl. klin. Wochensch.*, 1857, IV., p. 96), a conclusion cannot be drawn from the height of the temperature as to the severity of the fever. Similar febrile temperatures in the same individual during one and the same disease, as well as similar temperatures in different individuals in diverse diseases may be susceptible of very different estimations. The severity of the fever, that is to say, the resistance which a febrile temperature opposes to removal of heat, the rapidity with which a remission caused by withdrawal of heat is counterbalanced, diminishes a good deal even before its normal close. It is only the amount and duration of a remission produced by withdrawal of heat that is a certain measure for the intensity of the fever. ZIEMSSEN and IMMERMANN (*Kaltwasserbhl. d. Typhus*, p. 92) coincide with opinion, and SENATOR (*Fieberhaft. Process.*, p. 159) expresses himself in the same manner.

RIEGEL and ROSENBERGER (*Berl. kl. Wochen.*, 1872, No. 29 *et seq.*) advance other views upon a similar question. ROSENBERGER observed in the course of experiments upon the effects of local abstraction of heat in the same patient in febrile and the non-febrile states, as well as in various degrees of intensity of the fever, constantly similar differences; in opposition to LIEBERMEISTER, who found that the loss of heat in baths of almost the same temperature was greater in fever-patients than in healthy individuals. Recently, RIEGEL (*D. Arch. f. kl. Med.*, 1873, XII., p. 109), has discovered, relatively to the action of alcohol, that the lowering of temperature produced by this agent, at various elevations of the final temperature, is nearly the same as in the non-febrile state, and in low final temperatures it appears to be somewhat greater than in rising body-heat. So that it would seem as if there were a very variable effect!

ELEVATION OF TEMPERATURE OF THE LARGER PART OF THE BODY SIMULTANEOUSLY WITH LOWERING OF THE TEMPERATURE OF INDIVIDUAL PARTS may be caused by:

1. Irregular distribution of production of heat throughout the body.
2. Irregular cooling of the affected peripheral parts, in contrast with increase of heat in some internal parts.
3. Especially by difference in the fullness of bloodvessels.

Physiological contrivances make it possible that with normal production and loss of heat, the temperature of internal and peripheral parts shall vary only within certain limits, and that irregularities caused by accidental external conditions (the circulation being normal) shall be quickly corrected. Local refrigeration must, therefore, with relatively great losses of heat or with relatively small supply of heat, most easily take place in the extreme peripheral parts of the body, where deviations from the normal limits most easily arise. In a pure chill the heart labors sufficiently, and yet the external parts grow cold because of the hindrance offered to the entrance of warm blood by the contracted bloodvessels; in collapse the activity of the heart is insufficient, and peripheral parts must grow colder

whether heat-production be increased or not diminished, or whether the peripheral bloodvessels be enlarged or contracted.

LOWERING OF THE TEMPERATURE OF THE WHOLE BODY may be caused:

1. Through diminution of the production of heat, with normal, or increased, or not much diminished loss of heat.

2. Through increase of loss of heat, with lessened, or normal, or not much increased production.

3. By a combination of the above conditions.

It is usually not possible to assign, in a given case, the share of action to diminished production and increased loss of heat with anything like precision. A depression below the normal body-heat may make its appearance after the body has been normally warm, or after its temperature has been increased; and in the latter case, under certain circumstances, a fall to normal or super-normal values (as in collapse) may have the same meaning and consequences as the previous fall to sub-normal temperatures.

The certain demonstration of a reduction of heat-production below the normal amount is at the present time as impracticable as it is, according to what has been said above, to decide in a given case whether there is increase of production. Most probably it (diminution of heat-production) is, together with increased loss, the cause of febrile remissions and of defervescence, especially in rapidly progressing acute diseases. In many cases, in which it may have appeared right to assume reduced production, the diminished temperature may (according to the experiments of NAUNYN, referred to at p. 678) in part be owing to an increase in the loss of heat. Doubtless, heat-production must be made less by starvation; but in patients this influence of insufficient supply of food is certainly very often neutralized by opposing conditions, especially in fever. The circumstances connected with this subject are particularly complicated.

It is not only by the direct action of a sufficient degree of cold (HORVATH, *Med. Centrlbl.*, 1871, p. 531, was able to reduce the temperature of young dogs so that the thermometer placed in the rectum showed 6.6° C., 5.8° C., and even 4.8° C., and yet was successful in reviving them by means of heat,—a result hitherto not attained) in its various forms, such as baths, cold applications, ice-bags, cold air, that the heat of the body may be reduced, but also by the introduction of certain substances into the organism; and these are used more or less frequently in modern practical medicine, since the importance of antipyretic treatment has been appreciated. Among the substances referred to are especially quinia, digitalis, veratria, alcohol (BINZ). The mode of their not yet fully appreciated action is doubtless a complicated one; they act partly as cardiac poisons, and influence on the one hand heat-production, on the other hand loss of heat.

Most obvious are the depressions of temperature, that is to say, conditions which justify the conclusion that there is diminution of the production of heat, after the introduction of substances which influence and actually reduce tissue-metamorphosis, especially that taking place in muscles. Thus curare operates according to some authorities (RÖHRIG and ZUNTZ, RIEGEL), while others (VOISIN and LIOUVILLE, FLEISCHER) attribute to it the property of increasing temperature; nicotin (ROSENTHAL) and chloroform (SCHEINESSON) act in the same way. On the other hand, under pathological conditions increase of loss of heat has been shown to be a cause of important modifications of the body-heat, even causing death. Thus, for example, in extensive burns, in which BILLROTH (*Arch. f. klin. Chir.*, VI., p. 413), observed a temperature of only 33° C., in a man thirty-seven years of age. According to FALK (*Virch. Arch.*, LIII., p. 27), this refrigeration is the result of the extraordinary enlargement of the peripheral bloodvessels affected by the heat, whence increased size of the blood-stream with a local retardation of the circulation almost up to the point of stagnation, partly because cooled blood runs much more slowly through the tissues: in which condition loss of heat is specially increased, the more so if the epidermis is removed. The enlargement of bloodvessels takes place independently of nervous influence, as well of vaso-motor nerves as of the ganglionic apparatus in the walls of bloodvessels; it occurs rather in consequence of a diminution or abolition of the elasticity of the vessels and of the adja-

cent connective tissue, and in the larger bloodvessels also by heat-rigidity. Death results partly in consequence of great cooling of the blood, which lowers the excitability of the heart and that of the central nervous system, partly in consequence of the greater paralysis of the heart produced by increase of the vascular area. In a similar way, and not at all by the retention of certain substances in the body in consequence of arrested function of the skin, shorn and varnished animals die with enormous reduction of their body-heat. (LASCHKEWITSCH, *Arch. f. Anat., etc.,* 1868, p. 61.)

Among means of depressing temperature also belongs the fast-binding of animals, a measure employed in experiments, and hence practically important (HORVATH, BILLROTH). This acts partly by producing almost perfect muscular quietude, partly by exercising the same influence as simple exposure of parts of the body which are usually protected (especially the abdomen); thus increasing the loss of heat. The less constant body-heat of animals acts as an obstacle to quickly obtaining conclusive results in these experiments. Furthermore, according to MANASSEIN (*Arch. f. Phys.,* IV., p. 283), the reduction of temperature (0.81° C.) produced by swinging a rabbit in a certain way, for a period of fifteen minutes, does not depend upon increased loss of heat, especially because the minimum temperature is not attained until thirty minutes after cessation of swinging. Swinging produces a diminution of temperature also in feverish animals, though, like all other means, producing less effect when the body-heat is increasing than at the time of a fall of temperature.

Diminutions of temperature in morbid conditions, apart from unimportant and transitory elevations and depressions (p. 606), may best be considered under the heads of such as occur in the chill, in febrile heat, and in collapse. Doubtless these three states are variously composite groups of functional disturbances and of chemical and histological alterations as well, among which anomalies of temperature are most apparent, and appear to play the most important part. Many of the phenomena depend directly upon the condition of animal heat, and in many cases the most important alterations are those which may be directly referred to this. On the other hand, some of these alterations may be more or less independent; they depend directly upon the causes of the disease, and exert an influence upon the temperature, as for example, many of the previously-described anomalies of circulation, respiration, and of the nervous system. Still the influence of modifications of temperature upon the conditions in question is in most cases a much more decisive one than that of any other process. Thus a disorderly arrangement of facts is made impossible, and we are struck with the great conformity to law existing in the relations between constitutional anomalies and variation of temperature; and this conformity to law appears the more distinct the more carefully and precisely we observe disease.

Thus the CHILL presents itself as a complicated introduction to certain forms of disease: in some it almost invariably appears, in others it shows itself only with a certain intensity of the affection, and in predisposed individuals. When the last factor is strongly developed chills may make their appearance at times when, and in diseases in which they are usually absent. Chilliness shows itself most surely when the temperature of the trunk rapidly rises, so that there is produced in a short time a marked contrast with the temperature of the extremities; a contrast whose immediate removal is prevented by the above-described simultaneous, or almost simultaneous disorders of circulation. But the chill is not inseparably united to these conditions, and does not always come on when they are present.

In spite of marked contrast of temperature it may remain absent in individuals of slight personal susceptibility, and on the other hand may arise in susceptible persons without any such contrast; just as healthy persons, or those who believe themselves well, begin to shiver when exposed to various degrees of cold. Its (the chill) importance for the regulation of heat consists in that during its continuance (especially during the prevalence of the pyrogenetic stage, in which the characteristic phenomena of chill disappear), as well as just before the hot-stage proper, the loss of heat is limited, and that just at a time when the febrile changes in metamorphosis and the heat-

producing processes are in operation, and when abnormal sources of heat, as the muscles (shivering, chattering of the teeth), are producing copiously. Even with a less complete development, though with as long a duration, this stage may be the cause of marked accumulation of heat, though, to be sure, this is by no means sufficient to explain the hot stage as a whole.

In the HEAT OF FEVER there undoubtedly exists a certain relative equilibrium, though not an equilibrium at the level of normal conditions, but one which is determined by the newly-introduced pathological processes; hence sometimes large variations, though always with a return to a greater or lesser elevation of temperature, at other times a most remarkable constancy of body-heat (within a few tenths of a degree), in the so-called regular, continued or remittent course of fever, in paroxysms of intermittent fever, etc. If such a relative equilibrium is gradually established, and if it remains tolerably constant in spite of increase of the body-heat, it is conceivable, in accordance with what has been said above, that phenomena of chill should be wanting. During febrile heat there is a disproportion between abnormally increased formation and the not proportionately increased loss of heat. At the same time, the giving off of heat at the height of the fever may be always greater than normal (LEYDEN), and occasionally even greater than the febrile heat-production (SENATOR); but there may also temporarily occur a restriction of the loss of heat. Since the same condition of heat-production is simultaneously possible, the disproportion between the two is not at all times strongly marked.

During DEFERVESCENCE, especially when it is accompanied, as usual, by profuse sweating, the loss of heat is much increased; and by this means the superfluous heat which has accumulated during the height of the fever is removed, and providing that the equalization is a complete one, the equilibrium of the normal state is restored. In this stage the other symptoms produced by the febrile rise of temperature also subside.

COLLAPSE takes place in feeble states of the circulation, and its appearance is certainly very much favored by the occurrence of large losses of heat, whether heat-production be normal, or increased, or diminished. When there is debility of the heart, the heat produced in the interior of the body cannot be carried out to peripheral parts in a normal manner, and it is in those parts where the loss exceeds the supply. In case of simple large losses of heat, together with transitory feebleness of the heart, the prognosis is favorable, but, on the contrary, it is unfavorable when the circulatory power is irreparably weak.

Collapse appears as a relatively primary phenomenon, during the operation of severe poisons, as well as in consequence of strong impressions upon the nervous system; furthermore, during the intense chills of congestive (pernicious) fever, and to a certain extent after a fit of drunkenness. It makes its appearance secondarily during febrile heat under the operation of certain influences, during abundant losses of heat, copious sweats coincident with weakness of the heart, in predisposed individuals; also in the agony; and lastly, during the transition to recovery, especially simultaneously with excessive perspiration.

C. HISTORICAL SKETCH OF RECENT THEORIES OF FEVER.

Consult the critical account by WUNDERLICH, *Arch. f. Phys. Heilk*, I. et II.—TH. HIRSCH, *Die Entwickelung der Fieberlehre, etc.*, 1870.—E. SEGUIN, *Medical Thermometry, etc.*, N. Y., 1876.

Among all the various chapters of pathology there is none which reflects so clearly in all ages, the leading ideas of the dominant systems of medicine, as the then existing conceptions of the nature and causes of fever. WUNDERLICH says, " The doctrine of fever has always been the mirror of pathological systems, but it has also always been the pathognomonic symptom of their imperfection. The ancient doctrine of fever is little fitted to afford an explanation of the nature of fever, but serves rather to teach us the infirmities under which the pathology of that day was laboring."

Concerning the general conception of fever and its nature, or as would formerly have been said, its final causes, we find very confused ideas enunciated in various times, from which in the following paragraphs short selections are made.

HIPPOCRATES, free from all speculation, attached the greatest importance to the heat observed in fever, and named it accordingly; he designated it as an increase of the *calidum innatum*, tho originally present heat, the principle of life. This conception, although modified and distorted by his successors, remained dominant for nearly 2,000 years,—until toward the close of the seventeenth century.

During the middle ages the minds were principally occupied with the humoral-ætiological side of the question ; there were added ideas concerning changes of, and the presence of foreign materials in the liquids of the organism. Thus, according to FERNEL (1531), fever is a preternatural heat, thrown from the heart throughout the whole body. Its cause is threefold : simple increase of heat, as according to HIPPO-CRATES ; then heat from putrefaction, and heat from toxic infection. For PARA-CELSUS (1648) the *materia peccans* in fever is "sulphur and saltpetre, hence the disease is also called *morbus nitri sulfure incensi.*" In this ætiology, which was sought more or less exclusively in chemical and chemico-humoral processes, the fever itself was forgotten.

STAHL, according to whom all vital processes were controlled by a single principle, the Soul, conceived fever to be "an almost conscious motor, secretory, and excretory act for the removal of noxious matters," by which the general circulation was made stronger and the heat was increased ; SYDENHAM adding the aphorism, "fever is an instrument of Nature, by means of which she separates the impure parts from the pure." It was no longer important to answer the question, What is fever? but that other, What is its purpose? This doctrine prevailed during the whole of the eighteenth century, and we meet with it even now among the laity ; "it passes for a sign of deep medical philosophy" (WUNDERLICH). Later an expression was found which seems not less insidious than the abstract picture of a keen medical intelligence ; fever was called a reaction of the organism against noxious matters ; it was looked upon as an universal reaction, just as inflammation was a local reaction.

The first results of the application of the new doctrines of physics to the organism were the propositions which the Iatro-mechanists of the seventeenth and eighteenth centuries had advanced, and accordingly their school represents the beginning of positive medicine. They abandoned the exclusive regard in which the heat of fever was held, raised the pulse out of the symptom-group, and gradually introduced the movement of the blood into the notion of fever. This was especially brought about by BOERHAAVE and his school. The nature of fever was made to coincide with the immediate cause of the frequency of the pulse, was sought for in an irritation of the heart, or of the vascular system, or of the vascular nerves, or, lastly, by a complete confusion of all physiological notions, in an irritation of the blood ; in diagnosis the existence of fever was connected with the single phenomenon of frequency of the pulse, and upon this the plan of treatment was made dependant. "*Signum pathog-nomicum omnis febris est pulsus aucta velocitas*" (VAN SWIETEN, 1745). It cannot be doubted that this localization of fever in the vascular system or in a part of it afforded no explanation of its true nature. FR. HOFFMANN (1738), for whom fever was a gen-eral disease, picked out the condition of the heart and bloodvessels, and applied it as principle of classification to the whole of pathology. He at first distinguished between the "seat" of the fever, *i.e.* of the febrile symptoms, and "starting-point" of the febrile disease ; the former he placed in the heart, and besides in the central nervous system, especially the spinal cord ; the latter he found in various organs, most fre-quently in the stomach and intestinal canal. Thus it would seem that he, among the older writers, had best approximated to the modern explanation.

Later still, the displacement of the theories of the fluids and blood by the nervous pathology became still more complete ; certain phenomena were more generally desig-nated as functional disorders of the nervous system. Nevertheless, assignment of the part played by the nervous system, its centres, the liquids, the heart, and the bloodvessels, was arbitrarily and obscurely made, and differently set forth by the various authors. Among them the most remarkable is CULLEN, who first endeavored to construct a physiological notion of what occurs in fever ; and in so doing he cer-tainly looked upon chill and heat as cause and effect, and thought that, in fever, a spasm of the most external bloodvessels, resulting from diminished energy of the nervous centres, irritated the heart and arteries, and that this spasm continued until the cramped bloodvessels became relaxed and the spasm ceased. In this the expres-sion "spasm" does not mean anything more than a mechanical condition.

HALLER'S discovery of the irritability of muscular fibres led in the most remark-able way to the recognition of irritability as a mode of life, and to the interpretation of disease and of fever as changes in this property. The BROWNIAN system which for a very long time reigned in undisputed sovereignty throughout Germany originated in this. BROWN saw in all morbid states only a departure from the average irritability brought about by too great or too slight irritation,—sthenia or asthenia ; sthenic diseases with accelerated pulse constituted the pyrexias, asthenic diseases with the same pulse were the fevers ; and, consequently, these affections were treated by means of irritants. BROWNISM was only supplanted toward the end

of the eighteenth century by the numerous systems sprung from natural philosophy, which on the one hand added to sensibility and irritability (with a perversion of the original signification) reproduction as a third factor, and in a somewhat arbitrary manner referred all diseases to one of the three systems; and which, on the other hand, taught that an explanation of all diseases, and of fever in particular, was to be found in a mistaken application of the doctrine of polarity. In this way there ensued such an incredible confusion, that it would be useless to make a closer examination, because from all these speculations there was no advance gained for science in general, and for the doctrine of fever in particular: one definition may be worth while giving as an example. MARCUS, who had previously adhered most strictly to Brownism, says, in 1807, " Fever is always an affection of the electrical element in arteriality, by which this is made to contract." All fevers were diseases of irritability, and inflammatory states; they were distinguished only by the fact that inflammations proceed from organs, fevers from the system generally; he admitted a lymphatic, arterial, venous, and nervous fever.

As the result of so many, nearly always perfectly useless inquiries into the symptom and nature of fever, many became persuaded that the question under discussion was not capable of being solved. LIEUTAUD begins by saying: "What fever essentially is, is as yet enshrouded in the deepest darkness for human eyes." PETER FRANK does not trouble himself to give a definition of fever in general, but says: "Febrium origo et ratio proxima profundius quam ut oculo mortali distingui valent delitescit." "Febris certorum potius morborum umbra quam ipse morbus est."

In the meanwhile an improved state of knowledge had begun to show itself in France under PINEL, and later under BROUSSAIS. PINEL passes rapidly over the general definition of fever, as it had been previously arbitrarily deduced from the general ideas of a system, and says: "We must take care not to set up fever as a reality, or to study and define it as something independent. Fever is a purely abstract notion." It had been the custom to distinguish between fevers and febrile diseases. By the former were meant acute affections, in which, at the beginning at least, fever was the chief phenomenon (essential or simple fever), in which one part of the body was not mainly involved; the latter included local diseases with febrile symptoms, which appeared subordinate, secondary, and complicating, and which were thought to accompany the local affection. PINEL was the first to endeavor to ANALYZE the single symptoms in the forms of diseases considered as units by tradition, in order to learn what were the elementary phenomena, and he was thus enabled to give to the genera of fever sharper and simpler characters than was possible before him, and to which he felt himself obliged to return in his observations—a half step only, because the physiology of the day did not permit a deeper insight. In another way, however, he made a remarkable progress, following the general anatomy now for the first time formulated by BICHAT, by classifying fevers according to the apparently most affected organic system, and by establishing the similarity of phenomena in case of affection of parts having a similar texture. His HISTOLOGICAL DIVISION of fevers (*f. angiotenica*—with tension of bloodvessels, *f. meningo-gastrica*, *f. adenomeningea*—mucous fever, *f. adynamica*, *f. atactica*—with nervous symptoms, *f. adenonervosa*—with glandular affections) was undoubtedly incomplete and capricious, but it served to point out the way in which histology might be made useful to practical medicine in the future.

PINEL's doctrine of fever gave the impulse to the rapid development of French pathology under BROUSSAIS and his so-called physiological school, which, however, soon recognized the weak points in the doctrine, and combated it with success. B. borrowed from the Brownian school the notion of irritation, but soon identified this with active congestion and even with inflammation itself, thus confusing these three conceptions. According to him, fever is an irritation of the heart, produced by irritation of other organs, most frequently the intestinal canal. It did not escape him that in acute febrile diseases neither the organism as a whole nor a single organ is affected, but that usually several organs perform their functions badly, an observation which, before him, had led to the creation of arbitrary forms of disease which he strongly combated. He recognized that these were composed of a group of elementary disorders. As a bond of union which should combine the phenomena in the various organs and govern their sequence, he advanced his notion of sympathies, by which the various parts of the body are united, and through whose excitement by the primary irritation the secondary effects (irritations) are produced. The heart, intestinal canal, and the brain were distinguished by the strongest sympathetic union; any febrile irritation of one of these parts called forth a sympathetic irritation of these organs. And yet, the irritation by its transfer to another organ did not change

its nature; consequently the sympathetic irritations of the above-named organs always had a shade of inflammation. Lastly, intimately united with these views was his doctrine of the non-essential nature of fever, with respect to which he tried to prove that the starting-point of variously complex symptom-groups of the formerly so-called essential fever, was to be sought for in a local affection, particularly of the intestinal canal,—a gastro-enteritis. These doctrines were seized upon with avidity, but were also energetically disputed, to the great advancement of science, which was thereby led away from the caprice of the usual grouping of symptoms to the study of positive objects,—the exact observation of anatomical changes in the various organs. At this time exact observation began to take the place of phrases. Especially with regard to fever, the fact was made known that material changes were present everywhere. A persevering use of PINEL'S method of analysis led to the result that each individual local or febrile symptom was comprehended in its isolated significance, that in special cases it was attempted to discover the relation which the morbid states bore to one another and to the morbid cause, and, lastly, that by the help of physiology and of semeiological aids progress was made in the diagnostic recognition and naming of these conditions. Thus observation was henceforth diverted from the half capricious specific morbid ontology of former times to individual diseases.

The study of pathological anatomy placed medicine in the rank of the exact sciences. From that time on further demands were made on observation and theory; it became henceforth necessary that the phenomena during life and in the corpse should be noted with minuteness and exactitude, and that new knowledge should be accumulated in place of the older and almost useless records. The bases of PINEL'S genera of fevers crumbled more and more under the sympathies and the gastro-enteritis of BROUSSAIS, and in its stead was placed by BOUILLAUD the angio-carditis, which was supported by the anatomical researches of BRÉTONNEAU, LOUIS, ANDRAL, CRUVEILHIER, BOISSEAU, BOUILLAUD, and which was to be treated by venesection *coup sur coup;* while the physiology of fever was for a time wholly ignored. We consequently now meet with some more highly unrefreshing definitions. For ROCHE fever is only a word, by which increased frequency of the pulse and heat are designated; GENDRIN calls fever a disorderly disturbance of various functions; LOUIS designates fever as a conventional term for chill, febrile heat, perspiration, and changes of the pulse; PIORRY states that it generally cannot be at all explained; and ANDRAL does not enter into any discussion of its nature. Nevertheless, the opinion gradually became current in the third decade, that in fever the blood was altered, more especially in typhoid fever. This was after GASPARD had already in 1822 attempted to demonstrate the effect of the state of the blood upon symptoms of disease. ANDRAL and GAVARRET first, placing themselves upon a general standpoint, showed in 1840 that there was not present in fever a specific condition of the blood, and also that the assumption that such a state modified the symptoms of fever was inadmissible; the more so as febrile symptoms appeared fully developed in intermittent fever without any alteration of the blood. They suggested at the same time that the explanation of fever was to be sought for in something else. Afterward GRISOLLE, even in 1848, thought the origin of fever was sometimes in a local inflammation or functional disorder of an organ, sometimes in changes in the blood, and explained, just like the writers of the previous fifty years, that we did not know and could never expect to learn how it originated.

During this great advance of science in France, the German pathologists during the first part of the nineteenth century were still worrying themselves with speculations upon fever considered as an abstract generality, and we meet with such even later. Under the domination of natural philosophy the notion had developed that diseases, which in imitation of the descriptive natural sciences had been grouped in artificial or seemingly natural classes, genera, and species, were not to be looked upon as abstract ontologies, but as actually existing essentialities which attacked the organism like something hostile. Thus it was that to the natural school of the third decade (STARK, JAHN, less so SCHÖNLEIN) fever appeared the chief means of reaction of the organism against disease, of which reaction the organism made use to throw out critical evacuations, and by means of these to get rid of the disease itself, and in this connection the three stages of invasion, reaction, and crisis were distinguished. German physiologists were the first to lead minds back to the study of phenomena and to a reasonable comprehension of them, after they had been for a long time set aside, as was thought justifiable in fever; "the prototype of disease, in which the development of an ideally parasitic organism takes place most clearly, most legitimately, and most uniformly" (CARUS), strictly from the laws of healthy life. Reform first started in the study of intermittent fever; the opinion gradually gaining ground

that the nervous system is to a large extent concerned in the development of this disease. Strangely enough, SCHÖNLEIN and SACHS, adopting AUTENRIETH's idea that the course of many diseases, especially intermittent and typhoid fevers, was to be sought for in the ganglionic nervous system, to which since the time of BICHAT an important and independent *rôle* had been assigned, suggested that the former disease should be stricken from the list of fevers; and it was discussed whether it was a fever or a neurosis. Chiefly through KREMERS, who had observed the frequency of spinal pain in intermittent fevers, the opinion gained ground that the seat of this, and consequently the seat of even the non-typical febrile phenomena, was to be placed in the central organs, or, rather, in the spinal cord. The same opinion had previously and simultaneously been expressed in France (GEORGET, RAYER, OLLIVIER, MAILLOT), though not much attention had been paid to it.

The physiological treatise of J. MÜLLER contributed in an important manner to rendering ideas clearer, and to the revolution in opinions by the following laws. "The modifications of sensation, motion, and of organic functions, excretion and production of heat, which are characteristic of fever, are only comprehensible by the participation of such an organ as the spinal cord. Since fever is produced by nothing so easily as by changes in the activity of capillary vessels in any part, it is very reasonable to suppose that in fever certain impressions, starting from a severe affection of the organic nerves of any part, are transmitted to the spinal cord, and thence reflected through all the nerves." "This *umbra morbi*, which manifests itself in so many parts of the body, and which as a rule, perhaps always, has a local origin, is not simply connected with changes of the heart-beats; it exhibits itself in a complexity of symptoms which are united bound together only by means of the spinal cord." After the enunciation of these laws, destined to reform the whole doctrine of fever, it only remained to carry out in detail, by future investigations, what MÜLLER had shortly and in a general way expressed.

From among the numerous subsequent neuro-pathological theories of fever, it may be admissible to reproduce one (that of WUNDERLICH, *Arch. f. phys. Heilk.*, 1843, II., p. 6), with some details concerning its leading notions. All the phenomena which he considers as belonging to the febrile condition (such as general *malaise* and muscular weakness, altered sensibility and motility, disordered activity of the brain and organs of special sense, changes in the circulation, respiration, and digestion, as well as in the secretions and in nutrition, the altered objective conditions of temperature, as well as the subjective sensations of chill and heat) stand in causal relation to one another; they constitute an essential physiological unit, which, notwithstanding that its substance corresponds only partially with the usual changing and various views of practice and of nosologies, is still supported by facts. This being so, "fever" is consequently a grouping (*complex*) of associated symptoms, which are produced by a common cause, viz., an altered activity of the nervous centres, of the spinal cord chiefly; probably owing to a material change at that time wholly unknown. In the spinal cord there arises, sometimes directly and primarily (as yet remains to be proven by direct observation), sometimes in a reflected manner from other nervous parts, central or peripheral, sometimes, lastly, by the action of altered composition of the blood, a kind of "irritable weakness," that is to say, a state of heightened impressibility in which slight impressions are easily perceived and reflected, as well as always felt in an exaggerated manner, and in which movements following the action of a cause are easily interfered with by associated movements, and they are in great part removed from under the influence of the will. If this condition is aggravated by continued irritation, there at last occurs a spontaneous explosion of morbid sensations and movements—which, subjectively, does not recognize an external exciting cause, and in which, on the contrary, the centres seem to be wholly insensible to external impressions—the period of chill. After this there ensues a state of fatigue, dulness, and even torpor, which when it is moderate again causes increased susceptibility, but which when more severe shows itself as a true, or paralytic weakness. The hot stage, which in the great majority of cases ensues, is characterized by the cessation of that condition of the spinal cord which was at its height during the chill, and must be attributed to the development of local affections which keep up the morbid state of the spinal cord. If the remaining organs remain free from disease, the affection terminates in a short time, but it may be increased by the development of marked localizations; and a prolonged continued fever is never met with, unless such foci of disease are present. The special emphasis which is laid upon the hypothetical affection of the spinal cord in the fundamental notions of the theory, is employed by W. only for the exposition of the analogues of fever, which, notwithstanding their analogy to fever, are excluded from it in practice; as such may

be named: intermittent pain, so-called spinal irritation, tetanic attacks after injuries, morbid reflex movements under certain circumstances, neuralgia and spasm, nervous palpitation of the heart, and nervous delirium. The central affection may be generalized, or may be limited to one part, and, consequently, the phenomena dependent upon it may be general, or may appear in some parts of the body only; in which latter case the motor or the sensory apparatus, or even a single nerve-trunk, might be affected, and the further results (disorders of heat, secretion, of circulation) be modified or not appear at all. In practice we preferably call fever the general uniform affection, while we separate from it that which is really or apparently partial, and the sooner, the more it differs from the general affection.

What WUNDERLICH says of the varieties of fever, or about fevers with especial reference to the previously flourishing nosological systems, is particularly worthy of notice. " All attempts to arrange the interminable modifications of febrile diseases into exact classes have been wrecked, either because the classes were set up without any theoretical knowledge, or because a principle of classification was rigidly adhered to. Thus species have been retained, some of which are unnatural and forced, and others which allow of as endless modifications as the fever itself. A great error was committed in thinking that a single principle of classification would be sufficient. Febrile diseases present such numerous relations and aspects; of which one may be as important as the other, and none can be neglected at the expense of the others. Since, if with sufficient knowledge we place ourselves at all the various stand-points and study fever now from this and then from another side, we survey and comprehend the subject, and are elevated above the rigid species to which bigoted systematic writers cling. Rightly understood there is but ONE fever, though its connections are various. Important subdivisions can only be founded upon the degree of fever, its duration, the completeness of the symptom-group, the mode of recurrence (type), and, lastly, upon the part of the central organ which is affected. Besides this classification, which relates alone to the symptoms of fever, there are others not devoid of practical value; for example, that according to the general picture which the symptom-group offers (SCHÖNLEIN'S synochal, erethetic, and torpid fevers) or that according to causes, according to localizations and their peculiarities, according to the state of the blood, according to the degree of danger, according to symptoms, and especially according to the state of the nervous centres. But it must not be forgotten that any classification proceeding only upon one principle refers only to one aspect of febrile diseases, and that if one makes such a classification the standard and allows it to dominate his judgment and his thoughts, it is raised to the standard of a SYSTEM, and judgment and reflection upon concrete cases must be one-sided and false."

It is unnecessary to detail other important theories founded upon the same principle; what follows must suffice. According to LOTZE (1842) the term "fever" is intended to designate the symptom-groups which occur under circumstances which make them appear as the reaction of a general irritation of the nervous system, and the phenomena of which show themselves especially in the vascular system and in the vegetative functions. Hence fever consists in an irritation of the nervous system which does not involve the central organ directly, but through the medium of the sympathetic. For SPIESS (1844) this (the sympathetic nervous system) is the sole and direct excitor of fever, and is itself irritated by abnormal substances in the blood; it produces fever by its own independent power, and all cerebro-spinal manifestations are secondary. HENLE (1840) reached the conclusion, that the pathological alterations, in consequence of which febrile symptoms arise, are to be looked for usually in the spinal cord, and, when the special senses and psychical activity are much disturbed, in the brain as well. Fever, as such, is not a general disease, nor a disease of the blood, but an affection of the nervous centres. According to STILLING, this morbid state is produced by a foreign substance which is absorbed by the blood, and by the circulation of the infected blood, accumulations of blood are produced in the vessels of the spinal cord. In 1843 EISENMANN explained fever by saying that it consists in an irritation and subsequent feebleness of the vaso-motor centre, caused either by altered blood or by a peripheral irritation. In the same year HEINE stated that the irritation of the spinal cord in fever was always the result of a change in the whole blood. STANNIUS derives all the symptoms from an affection of the spinal marrow, but places the true origin of the fever in the blood or peripheral nerves. Yet ever so many of the most important of the neuro-pathological views of the fourth decade went to wreck on the fact, that the hypothetical lesion in the central nervous organ was not demonstrable.

The simultaneous labors in the field of organic chemistry (LIEBIG) must have exerted some influence upon the views of fever. LIEBIG'S own theory (1842) is as fol-

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lows. If in consequence of a morbid change of parts of the living body an amount of force is produced greater than is necessary for normal movements, there necessarily ensues an augmentation of a few or of all organic movements, and in consequence we have increased temperature, that is to say fever. The superfluous force which can only be consumed in motion is transformed into voluntary movements, and so produces the febrile paroxysm. G. HIRSCH remarked in 1843 : The fundamental symptom of fever is heat, produced by increased rapidity of the process of combustion in the capillaries, and is thus a purely chemical process. The chill is a nervous symptom and represents the reaction of the nervous system to a sudden impression, and is, furthermore, only something accidental. There is no reason to look for the immediate cause of fever in the nervous system. The importance of increased metamorphosis was likewise insisted upon by PH. VON WALTHER, NAUMANN, and others.

The older neuro-pathological theories of fever were finally overthrown by the renewed application of THERMOMETRICAL MEASUREMENTS, by means of which the fact that the BODY-HEAT IS CONSTANTLY RAISED in fever was placed upon a secure foundation, not to be shaken by any of the changes of theoretical views.

It was natural that the attention of investigators should be next directed to the investigation of the causes, the nature, and the mode of origin of the febrile rise of temperature. ZIMMERMANN constantly looked for these in localized inflammatory processes, an opinion which has been rejected as erroneous from all quarters. It seemed most probable to TRAUBE (1851, *Charité-Annal.*, II., p. 109), that the increase of animal heat, which is certainly in greater part the result of a process of combustion excited and kept up by the oxygen inhaled, is brought about by a weakness or paralysis of the regulatory centre for the heart, which lies in the medulla oblongata ; at any rate, he explained the reduction of temperature after the use of digitalis to an excitation of this centre, and the consequent slacking of the speed of the blood, with which the supply of oxygen must be diminished. We meet with a similar conception by VIRCHOW (1854, *Handb. d. Path.*, I , p. 26). Inasmuch as V. considers the blood as the vehicle of the febrile temperature, he finds the sources of this heat to be exclusively in an increase of the process of combustion, in which it is not at all necessary that with the entrance of larger volumes of oxygen the last products of oxidation of oxidizable substances should leave the body. The final cause of fever is, however, not to be looked for in the products of decomposition which accumulate in the blood, or else fever must arise after every meal by reason of increased combustion. For febrile heat is not a mere increase of temperature, but a rise of temperature having a special cause ; and this cause, according to all our knowledge, can be nowhere but in the nervous system. With respect to the connection between the nervous system and production of heat, it is to be remembered that febrile heat must be looked upon as the result of increased innervation of the nerves which serve for heat-production, as well as the consequence of DIMINISHED EXCITATION OF NERVOUS MODERATORS; the latter is all the more probable, because the whole febrile process so well exhibits the characters of weakness or of paralysis. Besides, it appeared unreasonable, bearing in mind the increased consumption of tissue in all parts of the body, and the evidently only secondary acceleration of the circulation, to localize the presumable state of weakness of the regulatory nervous system in a small part, about the seat of origin of the vagus nerve ; the assumption of a large number of morbid foci in the nervous system seemed most probable. Probably at the origin of fever we have to do with a state of abnormal tension in these nervous centres, produced by the fever-exciting cause, and which finds no escape by the usual channels. The more the power of the moderating centres is imprisoned, so much the more will the waste of tissues and consequently animal heat increase ; the longer this increase lasts, the more will fever become, what it was not at first, a general disorder, and equally so whether it is primarily produced, *i.e.*, directly through an alteration of the nerves, or secondarily, *i.e.*, in consequence of a distinct local lesion.

CLAUDE BERNARD also (1859) refers fever to the nervous system, but considers it an affection of the sympathetic nerve : the chill is a phenomenon of excitation, heat one of paralysis of this nerve. He says : when after section of the cervical cord of the sympathetic on one side the temperature of the head and the blood-pressure rise, temperature and the blood-pressure on the opposite side diminish, it would seem as if the organism could dispose of but a certain amount of force, so that when an increase takes place upon one side a decrease must occur upon the other In fever the sympathetic is in a similar condition, as is shown by those cases in which the blood in the veins flows out red and by jets, as after section of the sympathetic, and in which there is simultaneously a marked increase in the temperature of peripheral parts. These

facts can only be explained by the occurrence in fever of a state of equilibrium between the internal and external production of heat ; and there does occur a compensatory diminution of temperature in the chief sources of animal heat, the liver (B. estimates the normal temperature of the hepatic blood at 41.6° C.), and intestinal tract.   MAREY (1863) professes his belief in this theory of nerve-paralysis and compensation of heat, and adds to it, that with dilatation of the bloodvessels increased flow of nutritive material from the blood to the tissues, and greater oxidation, must occur.   In opposition to this, SAMUEL (*Die trophische Nerven*, 1860) designates fever as a condition due to a general state of irritation of trophic nerves, by which the increase of temperature is produced, and calls attention to the fact that the symptoms of fever are wholly absent in paralyzed parts, in which an irritation is impossible.   Furthermore, SCHIFF (1859) maintains against BERNARD's theory that we must not allow ourselves to be misled by the deceptive resemblance of symptoms of paralysis of bloodvessels to those of congestion, and to consider chill and febrile heat as conditions of irritation and paralysis.   For the palsy of vascular nerves, which of itself causes a rise in the temperature of the affected parts, at the same time prevents the action of any local changes by which the peripheral temperature is increased.   If, for example, we take animals whose vascular nerves have been paralyzed on one side by section of the corresponding sympathetic trunk, and excite fever in them, or overheat them by continued movements, the parts which in a state of vaso-motor paralysis are warmer in the non-febrile or quiescent state, become cooler and less vascular than the corresponding normal parts.   Hence, S. concludes that besides vaso-constrictor nerves there are also active vaso-dilator nerves, through whose agency febrile heat is produced, just as the chill is produced by the action of the vaso-constrictors.   Both are active processes, and independent of one another ; their frequent association only makes it probable that the irritations have a common starting-point. Lastly, JACOBSON and LEYDEN (*Centrlbl. f. d. med. Wiss.*, 1870, p. 259) showed that during fever the difference of temperature between the liver and the rectum fluctuates within the same limits as in the normal non-febrile state, and that, consequently, there is no foundation for the BERNARD-MAREY hypothesis of equalization of temperature.   On the other hand, BERNARD's theory seemed supported by the thermo-electrical researches of E. HANKEL (*Arch. d. Heilk.*, 1868, 321), who found the difference of temperature between the temperature of the axilla and that of the surface of the body, in the same individual, less in the feverish than in the non-febrile state.

Although, according to what has been stated above, VIRCHOW was also led, after a careful consideration of all known factors, to look for the explanation of fever in the nervous system, it may still be doubted whether it is necessary to conceive its activity as that of a directly controlling centre which modifies the production of heat and the amount of tissue-metamorphosis.

TRAUBE's (1863, compare p. 662) theory of fever ascribes to the nervous system, instead of the capacity of producing heat, that of checking refrigeration, by a direct or reflex tetanic contraction of the small arteries ; it also maintains the utility of the skin for the regulation of heat, as had already been done by BERGMANN in 1845.   If TRAUBE's view were correct, it would no longer be necessary to seek the hypothetical nerve-centre which regulates metamorphosis ; while, according to BUDGE (*Centrlbl. f. d. med. Wiss.*, 1864, No. 35), that controlling the muscles of bloodvessels seems to have been found in the crus cerebri.   However, this theory encountered almost universal opposition.   In the first place, AUERBACH (*D. Klin.*, 1864) called attention to the fact that increased animal heat may be caused besides by (1) increased production, as has been hitherto generally assumed, and (2) by diminution of loss of heat, as TRAUBE has it ; also by (3) increase of both production and loss with preponderance of the former ; by (4) diminution of both with preponderance of the latter ; by (5) increase of production with diminution of loss of heat.   And fever is not a simple thing ; doubtless these various conditions may occur in its course under different circumstances, at various times, and in various parts of the body, and the different meaning of the height of fever, and of the various forms of fever, may be dependent upon these factors.   He also makes the objection, that although the blood driven out of the small arteries can only remain in the capillaries and small veins, and by this the loss of heat must be again increased, yet, on the other hand, the increased frequency of respiration and of the pulse produces increased cooling by the lungs and skin.

Moreover, if the skin is moist and sweaty during the stages of heat and perspiration, which last much longer than the chill, the increased loss of heat is evident. Lastly, AUERBACH maintains that the undoubted increase of heat-production probably

results chiefly from combustion of hydrogen, which is furnished by the fat which is rapidly consumed in every fever, and much less from oxidation of carbon, as is usually thought. SENATOR rejects these assertions, because at the same time with oxidation of H there should also be more CO_2 produced, which is not the case; and, besides, these products of combustion cannot be increased because of deficient absorption of O. WACHSMUTH (*Arch. d. Heilk.*, 1865) asserts that it has not been demonstrated that a contraction of the arteries precedes, in point of time, the other phenomena of fever; and does this not to oppose the fact of contraction of the small arteries, but, on the contrary, against the reasoning that diminished loss of heat in fever is produced by this narrowing. And, besides, the fever continues, and the body-heat may even continue to rise, when the skin is perspiring profusely and the loss of heat must evidently increase. And, then, the state of the vascular system, proposed as highly characteristic of fever, is also met with in the insane. Lastly, emaciation and increase in the excretion of nitrogen were inexplicable without increase of heat-production, which, moreover, was sufficiently established by LIEBERMEISTER; so that a theory which assumed that impeded refrigeration was the only means by which a rise of temperature of febrile origin was made possible, must, at all events, be insufficient. LIEBERMEISTER (1865, *Prag. Vierteljahrsch.*, LXXXV.) showed that the surface of the skin in fever-patients during the heated stage possessed a decidedly higher temperature than in the normal state, and there could not be, as required by TRAUBE's theory, less heat brought to it; and, furthermore, that demonstrably it did not give off less but more heat to the surrounding medium than in the healthy state. The assumption of a contraction of the muscles of bloodvessels lasting weeks, such as must exist in long-lasting fever, was in contradiction to all physiological experience; and, then, besides, the fever-patient should, in consequence of diminished excretion of urine and of evaporation, become dropsical, which is well known not to occur. It is only during the stage of chill, in which all the peripheral arteries are actually contracted, that an increase of animal heat may thus be caused by diminished loss of heat; but yet there is, as shown with certainty by his researches, an increase of heat-production in fever, both in the period of chill and in that of heat. IMMERMANN also (*D. Klinik.* 1865), on the basis of calculations, expressed himself in favor of LIEBERMEISTER's opinion, that with an elevation of temperature amounting to 1° C. in a grown person (even in a chill), increase of heat-production is positively to be assumed, a statement which to-day almost no one contradicts. L. concludes with the following definition of fever: "By the name fever we designate a symptom-group, at the foundation of which is an elevation of the temperature of the body produced by a morbid general increase of metamorphosis." Finally, LEYDEN (compare p. 667) has overthrown TRAUBE's hypothesis in the most positive manner by the direct demonstration of an increase in the giving off of heat by fever patients, by means of calorimetric experiments. It is only since 1868 that through SENATOR some of TRAUBE's propositions have been again advanced in modified form, and with the concession of a moderate increase of heat-production.

After the rejection of TRAUBE's theory, it appeared necessary once more to determine precisely, for the explanation of the processes in fever, what share the nervous system had in their development. WACHSMUTH (l. c.) comes to the following conclusions upon this point: Neither increased heat-production nor diminished cooling can of itself produce fever. If either alone were sufficient, nothing could be more easily produced, or even possibly cured, than fever, but unfortunately the one is as difficult as the other. Rather there must be something superadded to increased heat-production or to arrested loss of heat,—the SUSPENSION OF PHYSIOLOGICAL COMPENSATION; in other words, in order that a person shall become feverish, it is necessary that the normal capacity of compensation for changing conditions of heat-production and escape of heat be lost. There is thus present in fever a DISTURBANCE OF THE REGULATION OF HEAT, and observation of patients shows that of the two possibilities, it arises by increased production without compensatory increase of cooling and not by checking of loss of heat, which leads to diminished production in a compensatory manner. Thus is it in the stage of fever-heat. However, observation of fever-patients teaches further that physiological regulation may not only be insufficient, or wanting, but that a true arrest of it may take place. The last is brought about by TRAUBE's contraction of the smaller arteries, as it occurs, for example, in the period of chill. The stronger and more distinct this contraction is, the more rapidly a marked rise in temperature takes place, until this has reached so great a height that the arrest is overcome, and the skin, in spite of its insufficient supply of blood, is heated, at the expense of internal parts, to more than the normal degree. At this time radiation from the surfaces increases in obedience to purely physical laws. If, at

length, the arterial spasm is relaxed, the functional disorder of the skin ceases, and the final lowering of temperature occurs with or without perspiration. According to this view, the sudden and rapid increase of body-heat is not the cause of the chill, but the changes in the skin which accompany it cause the rapid rise, and these changes may make their appearance at any period of the fever except when the great degree of heating of the skin prevents contraction of bloodvessels. The variations of animal heat in the course of a fever, the daily exacerbations and remissions are much more dependent upon tissue-metamorphosis than upon the nervous system, whereas the general type of the fever and its course are determined by the nature of the cause of the fever. With respect to the increase of metamorphosis present in fever, and of the allied production of heat, W., after rejecting BERNARD's vaso-motor theory, and ZIMMERMANN's inflammatory theory, comes to the conclusion that it is not necessarily dependent upon the nerves, and that an "irritation" of the blood may very well be its cause. This irritation may be looked upon as the effect of a ferment-like body, possibly ozone, especially since the discovery by SCHÖNLEIN and ALEX. SCHMIDT of the property of the blood, and of haematin of the blood-globules more particularly, by which they take up and transport the oxygen of the air. It is only necessary that the cause of fever should exalt the rapidity of diffusion of the solid and liquid parts of the blood, and thus effect an increase of the transportation of ozone, and that this does take place is taught by the composition of the urine. Furthermore, according to WACHSMUTH, there is not in fever a simple nervous moderation of heat-production in the sense of VIRCHOW, which, excited from somewhere, directly or indirectly arrests the processes of combustion in the body, or is left unbridled to itself, but a disturbance of the regulation of the normal equilibrium of heat, a mechanism complete in itself, by means of which the change from greater heat-production to greater cooling, and lessened cooling to diminished heat-production, and *vice versâ*, is facilitated, and the narrow limits of body-heat in the normal state maintained. Investigations have not yet made us more intimately acquainted with this mechanism, but they have had the result of determining its existence under very varied conditions. We can only say that—with the exception of the purely physical changes on the surface of the body produced by the heat itself—it is conceivable only as brought about by the medium of the nervous system, its ways and means being the preponderating changes in the circulation of the blood in the skin and lungs, as well as the insensible perspiration. To be sure, it does not seem difficult to designate the lesion of the nervous system in fever, yet opinions on this point differ as widely as if it were a question whether paralysis or increased activity of the nervous system is the lesion. From the peculiar contrasts in various provinces of the nervous system, from the existence of elastic, tonic, and muscular contraction of bloodvessels, and because of the dispute about vaso-dilator and vaso-contractor nerves and muscles, it is difficult to come to a satisfactory conclusion. At the present time facts make the assumption of a PARALYSIS of the heat-regulating mechanism most probable. W. considers the event in the case of febrile-heat to be a paralysis of the nerve-centre by means of which the innervation of the muscles of small arteries is moderated; for the explanation of the chill he falls back upon the contraction of vascular muscles, and he thinks that a subjective feeling of cold with marked elevation of temperature only occurs when this contraction takes place suddenly and forcibly, whereas with a slower and weaker contraction the increase of heat is less, and the sense of chill is wholly wanting. Possibly, however, the activity of this centre is not exerted specially upon the muscles of the small arteries, but chiefly upon the *tonus* of the tissues, and its innervation produces an alteration of the tissues collectively, including the smallest vessels, which with manifestations of turgescence and expansion opens to the blood-stream numerous channels, while its paralysis conduces to the opposite condition of collapse, such as so strongly characterizes the approach of death. The nervous factor in fever would consequently be a real paralysis, not so much of "vaso-motor" as of "sympathetic" fibres. Lastly, WACHSMUTH defines fever as "the result of at least two processes, one of which increases heat-production, the other paralyses regulation of heat through the nerves, and which when they occur together give rise to the succession of phenomena which constitute a febrile period."

The clinical observations of this period were wholly favorable to the assumption of the existence of a regulatory centre, as well as to its paralysis. This significance was especially placed upon the excessive temperatures at death, which appeared together with numerous signs of palsy of the nervous system, as well as after injuries of the spinal cord. WUNDERLICH, who likewise considered incomplete regulation as the cause of pathological modifications of animal heat, concluded, from numerous observations of extreme elevation of body-heat toward the end of fatal neuroses, that in

the unknown "changes in the nervous centres which cause death by so-called nervous exhaustion, there are factors by which its regulation is hindered or suspended.   Perhaps the tissues disintegrate prematurely in consequence of the cessation of the influence of the nervous system, and of chemical processes which rapidly produce heat."   It was now attempted to determine experimentally the seat of the regulatory centre, and in this way many important facts were learned.   TSCHESCHICHIN constantly observed, after section of the spinal cord in rabbits, a lowering of the body-heat, whereas an increase of heat followed a section through the medulla oblongata; and he concluded from these facts that the spinal cord may continue to perform its functions independently for a while after its separation from the brain, and that this independence is shown in an increased excitability of its centres, the activity of which is temporarily morbidly heightened and exhibits itself in increased animal functions, whereas, without section, all these functions remain under the control of the brain, which moderates them and holds them in equipoise.   Consequently, for him, fever is " a morbid increase of the activity of the spinal centres in consequence of a weakness or palsy of the moderating parts of the brain, whereby a series of chemical processes increase to a degree impossible while the functions of the brain are normal."   It must certainly not be overlooked that in observations upon dying patients, as well as in T.'s experiments, we have to do with exceptional conditions, which do not seem well suited to give a direct insight into the ordinary febrile state.   At all events, even in this, complicated conditions are involved.   This is also indicated by the results which NAUNYN and QUINCKE arrived at by similar experiments.   They conclude from them that there are in the spinal cord, besides vaso-motor fibres which exert a regulating influence upon loss of heat, and by whose paralysis after the operation an immediate dilatation of the bloodvessels of the skin and consequently an excessive loss of heat ensue, yet other fibres, which effect a regulating (inhibitory) influence upon heat-production in internal organs, and by whose division an increase of production of heat is made possible in the latter; it yet remains uncertain whether these are identical with the fibres which furnish innervation to the bloodvessels of internal organs.   A direct or reflex excitation of a hypothetical heat-centre by division of the spinal cord, they consider improbable.   The above-mentioned observations of HANKEL upon the increased temperature of the skin in fever are explicable by the help of these researches.

In the next few years the doctrine of regulation of heat was quite specially elaborated by LIEBERMEISTER, although it has, in the form in which it was presented by him, been subjected to numerous and well-grounded attacks.   In particular, L. maintains that there is a REGULATION OF HEAT-PRODUCTION ACCORDING TO EACH OCCASIONAL LOSS OF HEAT; the more heat is abstracted, the greater is the combustion. It is by such contrivances that the apparatus of regulation of heat is made perfect and becomes fitted for the performance of its extraordinary functions; and it thus becomes possible for the organs in the interior of the body to maintain their normal temperature in spite of the actually occurring great losses of heat.   This capacity is most probably made active through the nervous system, and it necessitates the hypothesis of an "excito-caloric system."   Even in fever-patients such a regulation of production according to loss of heat takes place, as is shown by experience in the use of cold baths, by means of which the production of heat, already increased above the normal, is excited to a much greater intensity.   To be sure, it would appear that its means are somewhat more restricted than those of the healthy, and that, for example, it is not capable of withstanding a strong refrigeration for so long a time.   In the further development of his idea, L. expresses himself as follows about fever. To the febrile state there belong necessarily the increased temperature as well as the increase of heat-production, but neither the one nor the other, nor both together, constitute the essence of fever, which rather consists in this, that REGULATION OF HEAT IS FIXED AT A HIGHER DEGREE OF TEMPERATURE.   A healthy person is distinguished from a fever-patient chiefly in that he regulates his loss and production of heat in equilibrium at about 37° C., and as far as is physically possible maintains this temperature, or regains it as quickly as possible.   The fever-patient, on the contrary, no longer regulates at 37 C., but for a given higher degree; yet by no means is the regulation of heat wanting in him.   Were this the case, he must behave with respect to his body-heat just like an animal in whom the spinal cord is separated from the brain.   To be sure, the condition in which such an animal is has often been called true fever, but the fact that in this state a moderate increase of loss of heat, by which the temperature of a fever-patient would not be noticeably altered, is sufficient to reduce the animal's body-heat far below the normal, would seem to contradict the assumption of such a similarity.   In what manner the establishing of

regulation at a higher degree, by means of which the organism has the decided ten-dency to continue at its high temperature of perhaps 40 C., is brought about, is at present absolutely obscure, and will not be better understood until after we shall know more about the intrinsic mechanism of regulation of heat in the healthy. All the most various phenomena which the symptom-group of fever embraces, all the peculiarities of the feverish organisms are naturally deducible from the change of place of regulation of temperature to a higher degree. In the stage of chill this higher location is suddenly effected ; in the stage of decrease of fever it does not descend from the previously high degree to the normal in a moment, but gradually, and often with oscillations.

LIEBERMEISTER's theory met with much opposition. It was accepted by ZIEMSSEN and IMMERMANN (*Kaltwasserbehandl. d. Typhus abd.*, 1870), though with the modi-fication that during the period of exacerbation the temperature is gradually elevated to successive heights by the postulated centre for regulation, while, on the contrary, during the period of remission it is established on successively lower degrees, and that the degree of temperature which happens to be present is retained with equal tenacity, whether it occurs in the period of exacerbation or in that of remission. BOTKIN (*Med. Klin.*, 1869) attaches more importance to the regulation of the loss of heat, and in this connection refers to the activity of an apparatus, the irritation or depression of which has an influence upon the secretion of sweat, in analogy to LUDWIG's experiments upon the secretion of saliva. IMMERMANN also (*D. Arch. f. kl. Med.*, XII., p. 179) argues in favor of the existence of such an apparatus. He assumes, with special reference to the frequent occurrence of a wholly dry skin with congestion (acute exanthemata, febrile turgescence), the existence of a nerve-centre, through irritation of which the secretion of sweat is arrested (as is the rule, for example, in fever), and through paralysis of which this secretion becomes pro-fuse (as in the agony, or under the influence of certain causes of fever—as acute rheumatism) ; and locates it in the medulla oblongata or just above it, in the neighbor-hood of LIEBERMEISTER's vaso-motor and excito-caloric centres. He believes that under the influence of fever-exciting causes usually all three centres are placed in a state of irritation, the conjoint effect of which is a rise of temperature with pheno-mena of ischæmia of the skin and with arrested perspiration, though under peculiar circumstances irritation of the vaso-motor centre and of the sweat-moderating centre as well, may be wanting, or nearly absent. These conjectures are to a certain extent supported by the investigations of LUDWIG and USTIMOWITSCH (*Ber. d. K. S. Ges. d. W.*, 1870, XXII., p 430), and of HEIDENHAIN, according to which not only a certain blood-pressure in the vascular net-work of glands, but also a certain nervous influence and excitation is necessary to the exertion of the glandular pro-duction ; and it is presumable that the febrile tissue-metamorphosis is capable of influencing the secretion of sweat in a variety of ways. For, at any rate, the absence or presence of sweat does not depend upon the febrile process, but upon the kind of disease and upon individual peculiarities. Lastly, with respect to the state of the temperature of the skin, it must be remarked that this, as E. HANKEL discovered by thermometrical means (*Arch. d. Heilk.*, 1873, XIV., p. 157), begins to rise at the beginning of natural or artificially produced perspiration, and remains elevated until its cessation, while the axillary temperature remains unchanged or is a little raised.

In the meanwhile the attempt had also been made, in conjunction with observa-tions on traumatic fever, to determine more exactly its origin and that of fever in general, by experimental means. In general less attention was paid, in these re-searches, to the regulating mechanism, than to the mode and course of the increased heat-production, whose occurrence was no longer doubted. Thus, C. O. WEBER (1865, BILLR. u. PITHA, *Chir.*, p. 599) understands by fever, " a general increase of tissue-metamorphosis united with heightened temperature, which is produced by poisoning of the blood by the products of decomposition of the tissues, acting in a ferment-like manner, and which determines a rapid decrease of body-weight." BERG-MANN also (*Pe'ersb. Zeitschr.*, 1869, XV., p. 16) states that with reference to a specific difference between the influence of products of putrefaction or inflammation upon the temperature, he was able to discover no difference, or only a difference of degree. He considers it possible that inasmuch as inflammation is only a mode of decomposi-tion, increased in quantity and more rapid, its products do not behave toward the organism as something completely heterogeneous, and thus its effects upon the gen-eral temperature are produced in the same manner as by the increased local temper-ature of inflammatory foci demonstrated beyond question by JOHN SIMON and WEBER. For the causes of fever do not open up absolutely new sources of heat ; they only increase the productiveness of those already present. B., looks upon the

blood as irritable, somewhat in the same sense as WACHSMUTH, and as irritated by the pyrogenic and phlogogenic products of the inflammatory focus. A return of the temperature to the normal follows the excretion of the irritament. BILLROTH (1872, *Arch. f. kl. Chir.*) considers as best suited to explain traumatic fever, the hypothesis, that substances are carried into the blood from gangrenous or inflammatory foci, which substances affect certain parts of the nervous system in such a manner, that henceforward the regulation of heat is destroyed, although it remains uncertain whether increased heat-production or diminished loss of heat occurs. The pyrogenic substances carried into the blood from the putrefactive and inflammatory foci, and between which there is no important difference in this respect, are not produced by the injury itself, but by septic processes in the wound. Whether the latter are only produced by a form of vibrio-gangrene, and the fever caused by fungi which enter the blood (HÜTER, KLEBS), has not yet been proven. It is, however, improbable that pyrogenic substances first produce an inflammation, and only cause a rise of temperature in consequence of it (ZIMMERMANN).

According to KLEBS (*Schweitz. Corrbl.*, I., 1871), the fever which accompanies the beginning of suppuration is produced by the entrance into the blood of phlogogenic elements which are produced in every suppuration, and which are probably identical with the ozone-carriers demonstrated in the spleen and in pus by K. Continued fever is caused by the continued importation of these substances, the end of the fever by cessation of the supply. It is presumable that the deleterious properties of pus, as well as those of the general infection produced by suppuration, are due to the presence of organized elements, most likely the fungus which he calls *microsporon septicum;* and during the development of which a substance is produced which has the property of exciting fever in the nutritive fluids. On the contrary, ALBERT and STRICKER (1871), deny that pus has any special pyrogenic property. P. NIEMEYER (*Memorab.*, 1873) may also be mentioned here as thinking that fever depends upon imperfect processes of combustion.

KLEBS and SAPALSKI (*Würtzb. Verhdl.*, III., p. 142), and NAUNYN and DUBCZCANSKI (*Arch. f. exp. Pathol.*, I., 1873) have opened up a most interesting perspective for our knowledge of fever. They found that injections of pus produced increased heat-production and increased loss of heat as well. The amount of the latter depends in an important manner upon the external temperature, and may well be the result of an effect of the pus upon the circulation of blood in peripheral parts; and K. in this connection calls attention to the increased loss of water which takes place, probably by increased evaporation. The increase of heat-production K., on the contrary, considers to be the result of the prolonged action of a peculiar chemical, ferment-like action of the ozone-bearing pus. NAUNYN holds the septic fever produced by experiments to be a vaso-motor phenomenon, which is produced by disorder of the function of certain parts of the central nervous system, and which conduces on the one hand to increased giving off of heat by an influence upon the cutaneous vessels, and on the other hand, to increased production of heat by an influence upon the circulation in the internal organs. The great similarity in the condition of animals experimented on to that of those upon which sections of the spinal cord have been made (*vide* p. 678) renders it very probable that a condition of paralysis is the cause of these disorders. In this way two factors are set free, which struggle for mastery over the result, as it were: whether this be a rise of body-heat or not, depends upon the preponderance of one of them, which do not necessarily always bear the same relation to one another. Accordingly, it can no longer be doubted that in really feverish states in man a lasting normal or subnormal temperature may be produced, if the factor of refrigeration assume the upper hand.

Most recently, two contributions have appeared which are calculated to rehabilitate some of the laws of TRAUBE's theory. First, HÜTER (1872 and 1873) published a theory, which he supports chiefly upon observations of disturbed circulation in the mesentery, tongue, and lung of the frog, after infection produced by fluids containing monads. Even in a few hours after infection, he found numerous small arterial and venous vessels filled with red blood-globules and excluded from the circulation; and in twenty-four hours one-half of the capillaries were in this condition. The occlusion of these bloodvessels is very often caused by adherent monad holding white globules. (Consult BIRCH-HIRSCHFELD, *Arch. d. Heilk.*, XIII., p. 389.) In the remaining vessels there is partly a slow and incomplete circulation, partly one which is normally fast and complete, the latter being a proof of the non-existence of palsy of the heart, by which the diminished rapidity of the whole circulation might have been explained. H. thinks, that this exclusion of such a large number

of bloodvessels from the circulation must cause an important diminution of the amount of loss of heat from the external surfaces (skin) and from the internal surfaces (the lungs), just as TRAUBE'S contraction of the small arteries, not proven to exist in all stages of fever, does. Exclusion of about one-half the bloodvessels from the circuit of the circulation, would represent a diminution of loss of heat by one-half, and in warm-blooded animals would suffice to explain the increase of temperature. The chill, with its sudden rise of temperature, indicates a sudden exclusion of numerous cutaneous vessels from the circulation. There is, moreover, no legitimate symptom of fever which is not capable of being sufficiently and simply explained by this theory. H. applies, in the first place, his theory to traumatic and suppurative fevers, and adds, provisionally, that increased production of heat may well play a part as well as diminished giving off of heat, and that every variety of fever must not be hastily subjected to the theory.

Lastly, SENATOR (1873) has given us a detailed exposition of his opinions upon the febrile process, as derived mainly from exact experiments upon metamorphosis. He expressly declines to give a definition of fever, because it appears doubtful to him that only one and the same process makes up what is generally understood by that term. His experiments, he states, are not applicable to all febrile diseases, but only to the greater number, especially the majority of acute infectious diseases; while other cases very surely, in still others probably comport themselves quite differently, and show nothing in common with fever except the increased temperature and its consequences. Rise of temperature is only one symptom, and does not constitute the essence of fever; its explanation has not yet furnished any theory of fever, because underneath this symptom very different morbid processes are combined, and because there are in fever other important processes independent of elevation of temperature. Among these he considers chiefly the special tissue-changes, as can be proven, in particular, by the different effects of pure pus and of pus treated with glycerine. He presumes that in the course of time it will be possible to divide fever, on the one hand, into one or several processes causing increase of temperature, and in others causing modification of tissue-metamorphosis. As important, though not sole sources of heat, he considers the demonstrable processes of oxidation; and for him the regulation of heat is nothing but the regulation of loss of heat. It (regulation of heat) takes place under normal conditions, in so far as it is not voluntarily produced, by changes in the frequency of respiration, and, besides, by the changing vascularity of the skin (regulated by the needs of the moment) and the therewith changing loss of heat. (Compare BERGMANN, *Müller's Archiv*, 1845.) In fever the utility of the skin is impaired to an important degree, because under the influence of the cause of fever an enormous irritability and irritation of its bloodvessels are produced, in consequence of which they are, from the beginning of the fever onward, occasionally contracted, and thus the equalization of superfluous heat is prevented. These periodical diminutions of loss of heat, together with a constant, though not great increase of heat-production, are the important causes of the febrile rise of temperature, and by them all the important phenomena of fever may, according to S., be explained in the most natural way. SENATOR'S exposition of the febrile process is simple, and is supported by facts which are almost universally acknowledged, a superiority which distinguishes it from many other theories.

XVII. MARASMUS.

CANSTATT, *Die Krkh. d. höh. Alt.*, 1839.—DAY, *A Pract. Treat. on Dis. of Advanced Life*, 1849. — DURAND-FARDEL, *Traité des malad. des vieillards*, 1854.— GEIST, *Klin. d. Griesenkrkh.*, 1857.—BUHL, *Z. f. rat. Med.*, 1857, VIII., p. 97.— CHARCOT, *Leç. sur les mal. des vieillards*, etc., 1868.

MARASMUS is the state peculiar to advanced life, but occurring at every age under morbid conditions, which consists in diminished nutrition and capacity of function of almost all tissues and organs.

Senile marasmus, and that which results from disease, premature marasmus, are hardly or not at all to be distinguished. In the earlier stages, in the marasmus of age, diminished nutrition and capacity of function affects almost all tissues and organs in nearly equal intensity, while in premature marasmus one organ or system, or another, is affected in a much greater

degree. In senile marasmus also the latter is often the case, but for the most part the initiatory disturbances escape the observation of both physician and patient.

In marasmus few changes are so constant that they can with certainty be regarded as consequences of it. With respect to most of these changes, no anamnestic or pathologico-anatomical distinction can decide the question of their origin from a preceding disease.

I. Senile Marasmus.

The CAUSE of senile marasmus is old age, the period after the seventieth year of life ("*senectus ipsa morbus*"). This form appears earlier and remarkably more quickly in persons of low vitality, from hardships, depressing psychical states, excesses, as a consequence of severe attacks of disease during the earlier years of life, and as a result of the use of powerful therapeutic means.

The SYMPTOMS of marasmus concern every system of the body.

The ORGANS OF CIRCULATION show the most frequent and furthest advanced changes.

The HEART becomes, as a whole, larger, especially broader, and somewhat thicker, and its openings somewhat wider. The valves are mostly thickened; the endocardium chiefly, in general or at points. The substance of the heart shows a stronger pigmentation, not infrequently fatty degeneration. The pericardium resembles the endocardium. The cardiac force is in general lessened.

The ARTERIES, usually the aorta most distinctly, likewise become larger and thicker: the thickness proceeds usually from an increase of all the tunics. Their elasticity and contractility are diminished, for the most part in consequence of the excess of connective tissue, often also through fatty degeneration and calcification, which, especially through the diminished nervous influence, is of importance with respect to the small arteries of various organs, of the heart itself, brain, large glands, as well as of those parts which are furthest from the heart (feet).

The VEINS become thick-walled, uniformly or irregularly wider, especially in the lower half of the body. Their elasticity is diminished.

The CAPILLARIES become in part wider, in part narrower to complete obliteration; their wall frequently shows fatty and pigmentary metamorphosis.

By all these conditions the circulation is in general affected injuriously. The heart's beat and the pulse are weaker; the latter in rigid arteries is remarkably hard. The sounds of the heart and arteries are feeble, and not infrequently modified. The heart-beat is, from unknown causes, quite often suspended. The mean frequency of the pulse rises to 75 and 80 beats. The temperature is lowered (see page 606). The blood accumulates, especially in the veins (so-called venosity), while the arteries are in general more empty. There exists a tendency to thrombosis of the arteries and veins (so-called marasmic thrombosis); in consequence of the former there results anæmic softening of the brain, and senile gangrene of the extremities. The influence of the vaso-motor nerves upon the arteries is probably always diminished, in consequence of which, influences of various kinds (changes of temperature, accidental and surgical wounds), without danger in the normal state, pass into inflammations and gangrene.

The BLOOD-MASS is diminished (senile anæmia). Almost all organs are anæmic. The blood itself is clearer, more fluid, poorer in solid constituents, especially in blood-corpuscles and albumen, richer in cholesterin; coagula-

bility is increased ("the fibrin increases"). In consequence there follow the general symptoms of chronic anæmia and hydræmia, especially cool extremities, etc., and the special signs of diminished function of all organs.

The larger LYMPHATIC VESSELS behave in general similarly with the veins. The conditions of the lymphatic capillaries are unknown. The LYMPH-GLANDS show simple atrophy in a varying degree to complete disappearance, sometimes transformation into fatty tissue, and calcification.

The SPLEEN behaves in a similar manner. It becomes smaller, dense, and tough, reddish-brown (so-called brown atrophy) ; its pulp may be so far lessened, that its tissue consists, in larger proportion, of trabeculæ and thickened vessels; its follicles are few, small, and even altogether wanting. The capsule is often irregularly thickened, so that the expansion of the organ is more or less prevented.

In consequence of these structural changes of the spleen and lymph-glands, the formation of colorless blood-corpuscles is probably diminished.

The ORGANS OF RESPIRATION likewise show constant changes.

The mucous membrane of the nose and pharnyx presents sometimes atrophy, sometimes hypertrophy of various kinds. The AIR-PASSAGES become wider, especially in consequence of the thinning of the mucous and muscular tunics, and diminished elasticity of their walls ; the cartilages becomes richer in fat ; not infrequently they are transformed into spongy bony tissue.

In the LUNGS so-called senile atrophy, or senile emphysema, is very often found, dependent upon a disappearance of the alveolar septa with destruction of the capillaries, thence giving rise, especially in the borders of the lungs, to very large air-filled spaces. The whole lung is smaller, less elastic, often rich in so-called false pigment ; here and there presenting atelectases, and other effects of various disturbances which may occur during a long life.

The intercostal spaces are, for the most part, correspondingly depressed, with anterior and lateral flattening, and general narrowing of the thorax ; the vertebral column is kyphotic, and, from the lessening of the intervertebral cartilages, shortened. The respiratory muscles, especially also the diaphragm, are, for the most part, atrophied.

The changes in the INTERCHANGE OF GASES in senile lungs are not certainly known : most probably there is a diminution in the oxygen taken, as well as of the carbonic acid given off, which are consequences partly of the conditions mentioned, partly of the diminished force, especially of the right side of the heart, partly of the diminished number of the red blood-corpuscles, partly of the impaired movement of the body, etc.

In consequence of these states, as well as of those of the circulatory apparatus, there is a shortness, with greater frequency and lessened depth of the respiratory act, diminished capacity of the lungs, diminished reflex irritability of the air-passages, lessened and difficult cough in disease, and consequently labored expectoration; finally, and on this account, the readier appearance of severer or deeper bronchitis, catarrhal lobular or lobar pneumonia.

The APPARATUS OF DIGESTION, as a whole, shows more or less distinct signs of atrophy ; often loss of the teeth, and, therefrom, atrophy of the jaws, especially the lower ; thinning of the whole digestive mucous membrane, already visible on the surface of the tongue, most marked in the small intestines, sometimes with black pigmentation and atrophy of the intestinal villi ; not infrequently thinning of the muscular coat, and, in consequence of it, marked general or partial dilatation of portions of the intestines.

In senile marasmus the gastric mucous membrane shows sometimes more or less numerous small yellow spots, *i.e.*, groups of glands with fatty contents (so-called *gastritis glandularis*, KLEBS).

Accompanying these conditions are difficult mastication and deglutition, diminished sense of taste, slower gastric and intestinal digestion, diminished resorption from the stomach and intestines, difficult defecation, sometimes alternating with diarrhœa. In addition there is a diminished consumption of nourishing foods (bread and meat) an account of the diminished function of the teeth, muscles of mastication, etc., and sometimes a more abundant use of less or non-nutritious substances. All these unfavorable circumstances are attended by a kind of chronic inanition (see p. 526).

Atrophies of GLANDS belonging to the apparatus of digestion occur in like manner : the glands proper of the mucous membrane in the whole length of the digestive canal, the salivary glands, especially the pancreas, liver, mesenteric glands. The liver shows the so-called senile or red atrophy, which consists in a diminution of the liver-cells with relative dilatation of the bloodvessels. The results of the more important functional disturbances, are, in detail, unknown : at all events there is diminished absorption of nutritious, etc., substances into the blood. The bile becomes richer in cholesterin.

Of the URINARY APPARATUS, the kidneys are not infrequently diminished in size, presenting atrophy of the urinary tubuli and bloodvessels with or without hypertrophy of the intermediate tissue, and atrophy of the mucous membrane of the urinary passages for the most part with atrophy of the muscular substance. In consequence of the renal changes the urine becomes scantier, darker, richer in coloring matter ; it also contains more urea and chloride of sodium, as well as extractive matters and odoriferous substances. The affections of the urinary passages are followed by a diminished contraction of the bladder, retention, or incontinence.

The BRAIN, especially the cerebrum, become ssmaller and firmer, tougher, poorer in fat and richer in water ; the convolutions are diminished in size. The sub-arachnoid space is usually enlarged, and the liquid of the cerebral cavities increased, and the meninges are for the most part clouded. The vessels show various forms of atrophy. The spinal cord behaves in a similar manner. Almost nothing is known respecting the sympathetic and the nerves.

Proceeding from this are, in general, a diminution of all psychical function, which may amount even to imbecility, loss of sleep, lessened subjective impressions during disease. Likewise from the resulting disturbances in the muscles and bones is explained the diminished movement of the extremities and internal organs, and on the other hand the trembling of the limbs, etc.

The organs of SENSE, sometimes all, sometimes a single one in a greater degree, show atrophy in its various forms. The cornea frequently presents the so-called arcus senilis (gerontoxon).

Of the MALE GENITALS, the testicles are found to decrease in size and suffer fatty degeneration, in consequence of which the semen is secreted more scantily, becomes thinner and for the most part poorer in spermatozoa. The tunics of the testes are often thickened. The prostate gland is sometimes atrophic, sometimes in a varying degree hypertrophic : the latter is the occasion of various disturbances connected with the evacuation of the urine.

Of the FEMALE GENITALS, the ovaries present atrophy of high degree. The uterus is either diminished in size or enlarged by secretions accumu-

lated especially in its body, and its walls are for the most part thinned ; its tissue is sometimes very tough, sometimes extremely soft, in which latter case its mucous membrane is often lacerated by hæmorrhages.   The pudenda show varying degrees of atrophy.   In the mammæ atrophy of high degree of the proper gland-tissue is found, sometimes with dilatation of the larger gland-ducts and replacement of the gland-substance by fatty tissue.

All these states are commonly followed by decrease of the sexual functions and their final disappearance, for the most part much earlier in the female than in the male.   No noteworthy pathological conditions result therefrom.

The BONES, most strikingly the tubular bones and vertebræ, remain of normal size or become smaller (excentric or concentric atrophy).   In the former and much more frequent case the compact tissue wall is thinned, and in places entirely disappears ; sometimes it remains of normal thickness, but is very porous ; the bone-corpuscles become wider, and the basis-substance poorer in organic substance.   The spongy substance likewise becomes more scanty in its bony constituent, the diploë may almost disappear ; the medullary spaces become everywhere wider ; the yellow marrow is for the most part transformed into the red ; or like the red it becomes softer, more vascular, or anæmic and œdematous.   The cartilages show various degrees of atrophy, especially metamorphosis into fibrous substance or into bone, or they calcify ; those of the joints are thinned, the joints themselves become drier.   The sutures between the bones of the skull disappear. In consequence of all these conditions, the solidity of the bones is diminished, and they break more easily ; movable bony parts, especially the vertebral column, become less flexible ; the latter shows kyphosis.

The MUSCLES are scantier, especially in proper muscular substance, richer in pigment, poorer in fat, more easily lacerated.   The flexors mostly preponderate, and on this account the articulations, most distinctly the fingers, are bent.   Their electric contractility is diminished.   The tendons are drier, and often shorter.

All motion becomes slower, and more awkward : not merely that of the body and extremities, but also the movements of respiration, voice, mastication, etc.

According to RANKE, there is a relative increase of apparatus of motion and decrease of the glandular apparatus with age ; tissue-metamorphosis rises and falls with the increase and decrease of the whole glandular apparatus in relation to the organs of motion.

The SKIN becomes thinner, in the white races richer in pigment, dirty yellowish, in the colored races poor in pigment.   The epidermis becomes drier, thinner, and scales off irregularly (*pityriasis senilis*).   Its stratum Malpighi becomes richer or poorer in pigment.   The corium itself loses its vascularity, moisture, and elasticity.   The nails become striated, deformed, brittle ; the hairs become blanched, drier, atrophic, and fall (*calvities senilis*). Sebaceous and sweat-glands become smaller, with less capacity of function : the skin is less oily, and perspiration diminishes.   Through all these conditions the function of the skin becomes manifestly diminished.   From unknown causes there is found not infrequently a peculiar hyperæsthesia (so-called *prurigo senilis*), sometimes very numerous boils, retention-tumors of various kinds of the sebaceous glands, teleangiectases, hypertrophies of the skin, etc.

The subcutaneous fatty tissue is almost always diminished, darker and more horny.   The connective tissue especially becomes drier.

See FLEMMING, *Arch. f. micr. Anat.*, 1871, VII., p. 328.

The above-mentioned properties of the skin, muscles and bones explain the known peculiarities of the external habitus in senile marasmus, especially of the face and hands. Even the length of the body decreases 6 cent. and more ; likewise the weight of the body by 6 kil., and more.

Through all the anomalies stated there arises a diminished resistance to injurious influences of every kind, and therefore a greater tendency to disease; and, further, a less resistance to morbid processes, to therapeutic measures (medicamentous and surgical), to bloodletting and hæmorrhages especially, and thereby a greater mortality.

2. Marasmus as a result of disease.

A general representation of this marasmus is impossible ; it is much more necessary, in individual cases, to look for its causes. With respect to this, and especially noteworthy, are :

Lowered vitality : in children born prematurely, or of diseased parentage (tuberculosis, syphilis, losses of blood, sometimes severe acute diseases, etc.) ;

Deficient or unsuitable nourishment, occurring more often especially in sucklings and small children ;

Difficult taking of food from various diseases of the mouth, throat, œsophagus, cardiac orifice ;

Diminished resorption on the part of the stomach or intestines (so-called *atrophia mesaraica*, etc.) ;

Diminished function of the so-called blood-forming organs (lymph-glands, spleen—liver in retention of bile, etc.—bone-marrow ?) ;

Hæmorrhages, losses of albumen, diabetes ;—severe general diseases, especially chronic tuberculosis, syphilis ;

Long continuing moderate or occasionally high fever ;

Some diseases, in which, from causes more or less unknown, there is an especially striking marasmus present : *morbus Addisonii, m. Basedowii* [Graves' disease—Ed.] ; goitre in the short-lived.

Therapeutically there are occasionally conditions, which should be considered in this place : for example, hunger-treatment, Banting treatment, "dry" treatment, etc. Hunger-treatment is, in important particulars, like the condition described under the head of chronic inanition (p. 534). For details upon the Banting cure, *vide* p. 544.

The symptoms of this form of marasmus are various, according to the nature of the underlying affection. At first they consist of the signs of acute or chronic anæmia of inanition (*vide* pp. 533–4), or those of anæmia succeeding hæmorrhage (p. 526), or of hypalbuminosis (p. 538), etc. After long duration there are allied to these more or less striking disorders of various organs, sometimes in all to a similar extent, sometimes especially in one or another. More especially striking are the symptoms as exhibited in convalescence from severe acute diseases, especially typhoid fever (wasting of the skin, hair, muscles, sometimes of the intestinal canal, etc.), and in some chronic affections, especially diabetes mellitus (*vide* p. 578), sometimes in chronic cancer, granular liver, chronic swelling of the spleen.

The issue of marasmus depends upon the nature of the disease causing it.

XVIII. HÆMORRHAGIC DIATHESIS.

Virchow, *Hdb. d. Path.*, 1854, I., p. 239 ; *Deutsche Klinik*, 1859, No. 23.—

GRANDIDIER, *Die Hämophilie*, 1855.—LEMP, *De hæmophilia nonnulla adj. morbi specimine rariori*, Berl. Diss., 1857.—WAGNER, *Die Fettmetamorphose des Herzfleisches*, 1864; *Arch. d. Heilk.*, IX., p. 497; X., p. 337.—KAPPELER, *Ueber Purpura*, Zurich Diss., 1863. [LEGG, *A Treatise on Hæmophilia*, Lond., 1872.—ED.]

Compare the literature of Hæmorrhage, p. 210; of Scorbutus, etc.

Under the general name of hæmorrhagic diathesis, are grouped a number of conditions, in which there occurs from different vascular areas a bleeding unexplained by any of the known causes of hæmorrhage (mechanical causes, changes in the texture of bloodvessels, congestive or accumulation-hyperæmia).

The forms of disease belonging to this group are sometimes primary and well characterized: as, for example, the bleeding-sickness or hæmophilia, true scorbutus, the *morbus maculosus Werlhofii, purpura* or *peliosis rheumatica;* sometimes these affections exhibit transitions into one another; sometimes similar conditions make their appearance in consequence of other well-marked diseases (acute exanthemata, typhoid fever, pyæmia, icterus, diseases of the spleen, etc.), after the administration of several medicines (iodine, mineral acids, etc.).

In many of the above-mentioned affections remote and exciting causes are known. Thus, in the case of hæmophilia, inheritance, especially in the male line; for scorbutus, restricted diet (want of fresh meat and vegetables), cold, dampness, muscular exertions, depressing psychical impressions. The hæmorrhagic diathesis shows itself only occasionally, sporadically or in the course of epidemics, in other diseases, as measles, pharyngeal diphtheria, etc.

Several endemics, especially in houses of correction, are in favor of the identity of *morbus maculosus Werlhofii* with scorbutus; in many of the cases there was only an affection of the palate and gums. in others the usual *morb. mac. W.*, in some large ecchymoses, and in others yet hæmorrhages in the muscles, and lastly in some hæmorrhage under the periosteum. Thus it was in the endemic in the prison at Wartenburg, described by WALD (*Vierteljschr. f. ger. Med.*, 1857, XI., p. 45).

BAUER (*Deutsche Klin.*, 1868, No. 35) met with certain families of which individual members were affected with purpura at a certain age. Hence he infers a relationship between *morb. mac. W.* and hæmophilia.

Not one exciting cause common to the various conditions grouped under the title of hæmorrhagic diathesis, is yet known. It is most likely that different causes are operative in the various conditions. In this connection may be named: traumatic influences, which in predisposed individuals may be so insignificant as to be overlooked by the patients (in hæmophilia, in many instances of bleeding into the muscles or from the gums, in scorbutics); congestive or collateral hyperæmiæ which subside so rapidly that the patient does not observe them, or which involve parts which furnish few symptoms or none at all.

To this category belong the small hæmorrhages of internal and external organs which occur in the course of ulcerative endocarditis: they are caused by capillary emboli.

The hæmorrhages which take place in consequence of accumulation-hyperæmia (*Stauungshyperämie*), which have been recently exactly described after microscopic study by COHNHEIM (*Virchow's Arch.*, XLI., p. 220), do not belong to the hæmorrhagic diathesis (*vide* p. 186).

In cases of hæmorrhage like those mentioned *supra* we often find, and almost equally do not find acute or chronic alterations in the walls of the

bloodvessels, functional, or chemical, or anatomical in nature, and most commonly fatty metamorphosis. And, in the first place, the degeneration of the vascular walls may be the consequence of the hæmorrhage or of the simultaneously present general anæmia.

Many think that the frequent hæmorrhages in acute poisoning by phosphorus are caused by fatty degeneration of bloodvessels (KLEBS, BOLLINGER).

In hæmophilia as in chlorosis the narrowness and great elasticity of the arteries may so much increase the blood-pressure in the capillaries, that thereby a predisposition to hæmorrhage arises, and the lacerations which occur are kept open (VIRCHOW).

Besides, a disproportion between the capacity of the bloodvessels and the amount of blood has been considered a cause of hæmorrhage.

If at the time of a greater production of blood the vascular system is very small and has only a small capacity, the blood-pressure must increase in the aortic sytem, not only in the direction of the heart, but it also attains a considerable height in peripheral parts. Nearly all cases of hæmorrhagic diathesis, or of hæmophilia, which have been studied in the last ten years have presented this condition of the vascular system. The AUTHOR considers this explanation admissible in the excessive hæmorrhages which occur at the menstrual period in chlorotic girls (*Beitr. z. Gebrtsh. u. Gynäk.*, 1872, I., p. 323).

Disease of one organ in particular and the hæmorrhagic diathesis have often been observed together. In these cases the affected organ was the heart (fatty degeneration); or a glandular organ (liver, kidneys), by lesion of which certain injurious substances were formed in the body, or the excretion of such substances from the body was prevented. Or there were severe diseases of the stomach and intestinal canal, with impeded absorption of nutritious substances.

Cases of this kind have been reported by the AUTHOR (heart and internal canal), by KOPPELER (kidneys), by HENOCH (intestinal canal). Apart from what has already been described (p. 348), I found in a second fatal case of *morbus maculosus* peculiar gangrenous foci in the intestines. Compare Leucocythæmia (p. 545) and Icterus (p. 550).

Diminution of the quantity of fibrin in the blood (hypinosis so-called), which has so often been considered as the cause of the hæmorrhage, cannot be such ; for in tolerably numerous cases of scorbutus, in some fatal cases of hæmophilia and chlorosis, the blood has been found especially rich in fibrin. This condition (hypinosis) may as well be a result of the hæmorrhage ; and the same is true of the diminished coagulability of the fibrin.

The increase of red blood-globules in the blood often causes hæmorrhage in various organs, or hæmorrhage (arrested with difficulty) externally after injuries (*vide* p. 545).

That chemical substances may occasionally be the cause of hæmorrhages has been certainly demonstrated by numerous experiments on putrid infection ; but we are not well acquainted either with the nature of the substances or their mode of action.

GASPARD (*Mém. sur les mal. purulentes et putrides. Journal de Phys., par Magendie.* 1822. II., p. 1 ; 1824, IV., p. 1) showed by numerous experiments, that the introduction of putrid substances into the body, especially in the veins, produced hæmorrhages in the most various organs, particularly in the intestines, lungs, heart, subcutaneous areolar tissue, gall-bladder, intestinal mucous membrane, etc. STICH insists most upon the intestinal hæmorrhages. VIRCHOW has confirmed GASPARD'S statements by his own experiments.

As regards the addition of a number of salts to the blood, GASPARD thinks ammonia peculiarly efficacious; in favor of this view are some foreign experiences, while others are opposed to it. Others blame the accumulation of soda- and potassa-salts, etc., because after the continued use of salted food, after the injection of carbonates in the blood, hæmorrhages appear. GARROD, on the contrary, considers the want of potassa-salts as the cause of the hæmorrhagic diathesis. The same is true of acids, alcohol, phosphorus.

O. WEBER Pitha-Billroth, Hdb. d. Chir., I., p. 126) observed numerous ecchymoses after the injection of water containing sulphuretted hydrogen.

PRUSSAK (-STRICKER, Wien. Acad. Sitzsber., 1867, LVI.) noticed a copious escape of red blood-globules (whole ones as well as pieces) through unaltered bloodvessels in frogs, perhaps also in rabbits, which had received injections of large quantities of solution of common salt in the blood, or had been placed for a long time in a strong solution of the same. COHNHEIM (Unters. üb. d. embol. Process, p. 27) was unable to verify this.

The SYMPTOMS of the various affections belonging to this group depend chiefly: upon the causal influences as in scorbutus, or upon the primary disease as in acute exanthemata; furthermore upon the hæmorrhages in internal and external parts, and the various local and general disorders caused thereby. The latter are more or less referable to general anæmia and hydræmia (vide p. 518 and p. 538). As regards the composition of secretions in this condition we want exact experiments.

The explanation of many symptoms is unknown: thus in the case of the rheumatic pains which precede these affections; those of scorbutus, etc. Usually there is only a small secretion of sweat. In the same way, even the post mortem examination does not afford an explanation of the severity of the cases (many acute cases of so-called hæmorrhagic diathesis).

DUCHEK (Oest. Jahrb., 1861, XVII., p. 39) found that in scorbutus, during the increase of the disease, all the constituents of the urine were diminished; potassa less so relatively than soda, so that the latter seemed relatively increased.

LEUDESDORF (Med. Centrlz., No. 80 et 82) describes a case of land-scorbutus in which the ecchymoses occupied only one-half of the body.

GARROD places the value of vegetable diet in the contained alkalies. From a direct estimation of the amount of potassa in the blood he believes that he has demonstrated the diminution of this substance. Still, this may well occur in consequence of diminished supply of food in general.

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TABLE OF EQUIVALENTS

OF

METRIC MEASURES EMPLOYED IN THE WORK.

MEASURES OF WEIGHT.

1 Gramme (gr.)   =   15.434 Troy grains.
1 Kilogramme (kil.) = 15,434.023   "   = 2 lb. 8 oz. 1 ʒ . 14 grains Tr.

MEASURE OF CAPACITY.

1 Cubic centimetre (C. cent.) = .061028 cubic inches = 1 gr. of distilled water.

MEASURES OF LENGTH.

1 Millimetre (mm.)   = 0.03937 inches.   [scopists).
1 Micro-millimetre (mmm., or μ) = 0.0003937 "   (standard adopted by micro-
1 Centimetre (cent.)   = 0.3937   "
1 Metre (M.)   = 39.3710   "   = 1 yd. 3.37 inches.

THERMOMETER SCALES.

1 Degree Centigrade (° C.) = 1.8° Fahrt.
To convert Centigrade into Fahrt. multiply by 1.8 and add 32.
Normal temperature in axilla = 37 ° C. = 98.6° Fahrt.

For full tables consult:

U. S. Dispensatory, and Pharmacopœia of U. S.
DUNGLISON, Medical Lexicon, 1874.
H. C. WOOD, Treatise on Therapeutics, Phila., 1874.
E. SEGUIN, Medical Thermometry, N. Y., 1876.

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Plate III.—Anterior plane. *Right side:* Superficial Muscles. *Left side:* Superficial aponeuroses. Plate IV. —Anterior plane. *Right side:* Muscles of the second layer. *Left side:* Muscles of the third layer. Plate V. —Posterior plane. *Right side:* Superficial Muscles. *Left side:* Superficial aponeuroses. Plate VI.—Posterior plane. Second and third layer of muscles. Plate VII.—Lateral plane. Superficial and deep muscles. Muscles of the os hyoides. Plate VIII.—Diaphragm. Interior of the trunk, muscles of the lower jaw, of the tongue, velum palati, and of the pharynx.

ANGIOLOGY.

Heart, lungs, arteries, veins, and lymphatics. On the different figures are indicated the points at which compression on the ligature of the vessels is effected, and in regard to the veins in particular, the proper points for performing venesection.

Plate IX.—Interior of the trunk. Heart, lungs, and their envelopes. Large vessels. Plate X.—Vessels of the thorax and abdomen, azygos vessels, cerebral and spinal venous sinuses. Plate XI.—Anterior plane. Sub-cutaneous vein, and deep vessels. Plate XII.—Posterior plane. Superficial veins, and deep vessels. Plate XIII.—Lateral plane. Partial figures, internal maxillary and internal carotid vessels, &c. Plate XIV.—Lymphatic vessels.

NEUROLOGY.

Plate XV.—Anterior plane. Encephalic nerves. Nerves of the extremities. Plate XVI.—Posterior plane. Studies of the ganglions and their nerves. Studies of the fifth and seventh cerebral pairs. Plate XVII.—Brain, Spinal marrow, and envelopes. Organs of the senses. Larynx.

DIGESTIVE APPARATUS.

Plate XVIII.—Alimentary canal, stomach, intestines, chyliferous vessels, peritonæum. Plate XIX.—Stomach, liver, pancreas, spleen, kidneys, supra-renal capsules, bladder. Abdominal venous system. Great sympathetic and pneumogastric nerves. Plate XX.—Complete study of the perinæum in both sexes. Male and female organs of reproduction. Embryotomy.

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Plate IV. Physics of light and vision.
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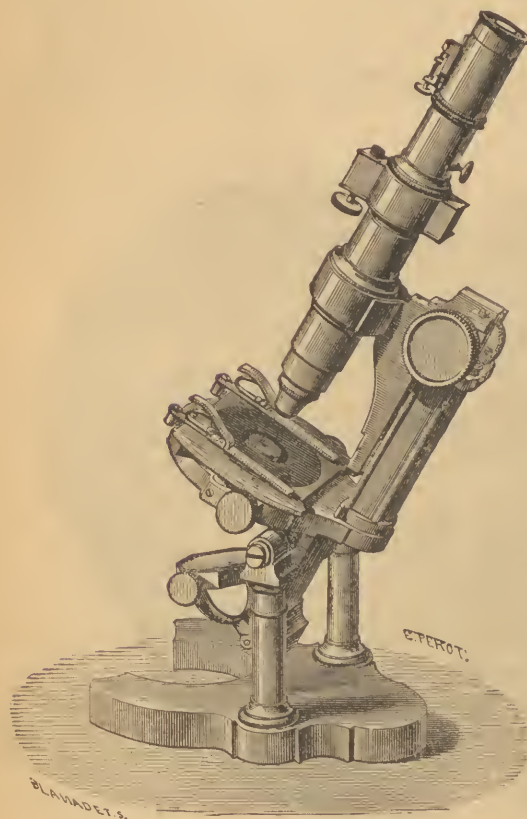
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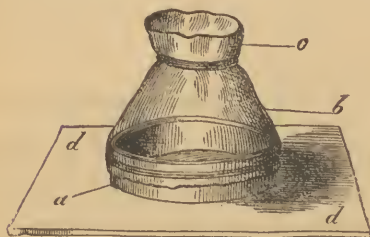
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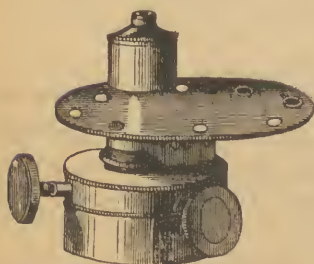
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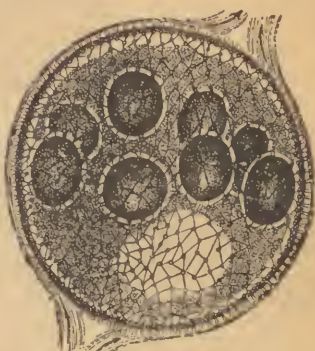
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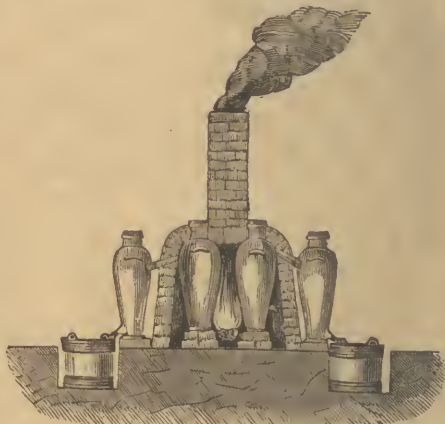
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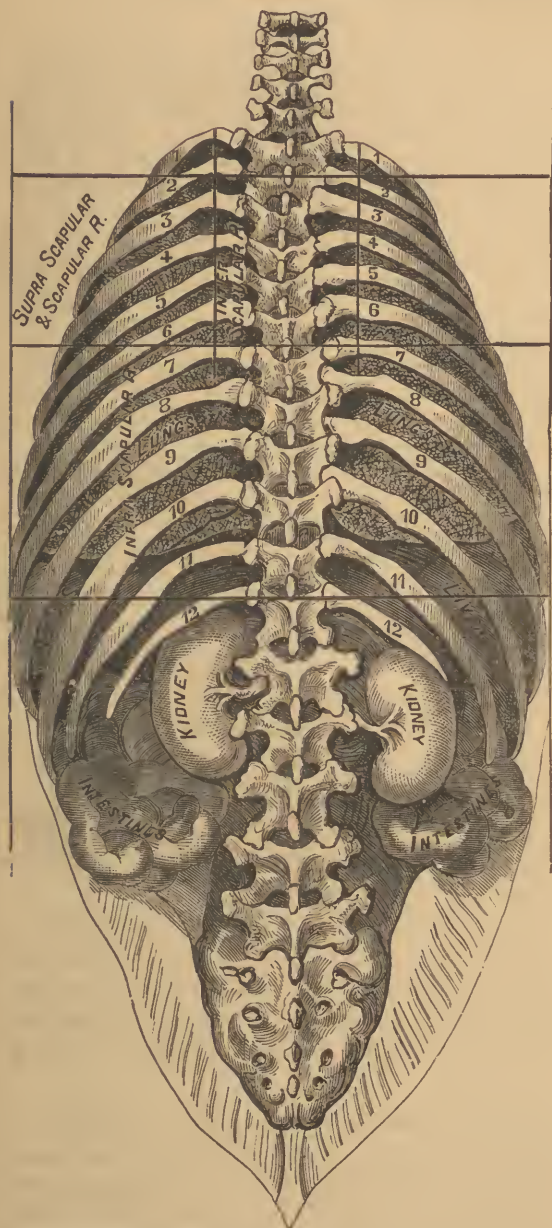
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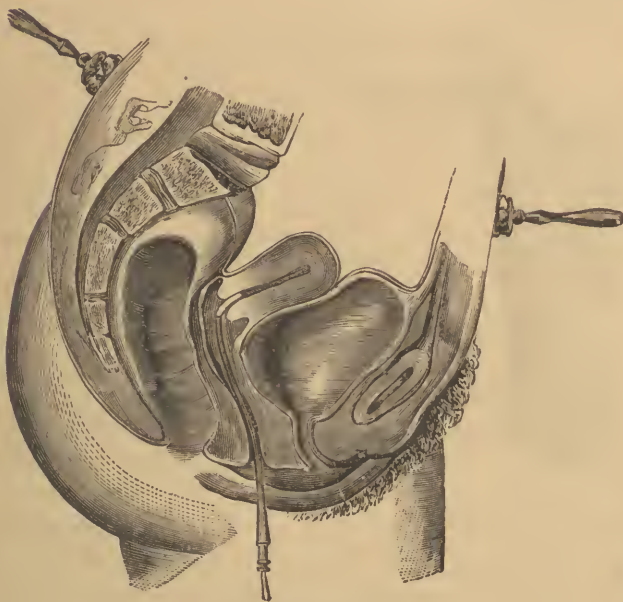
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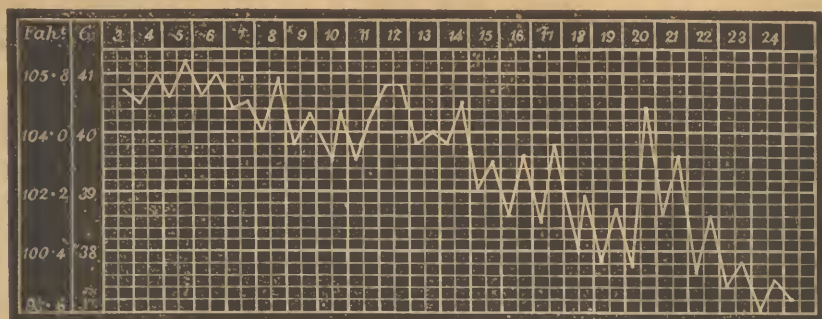
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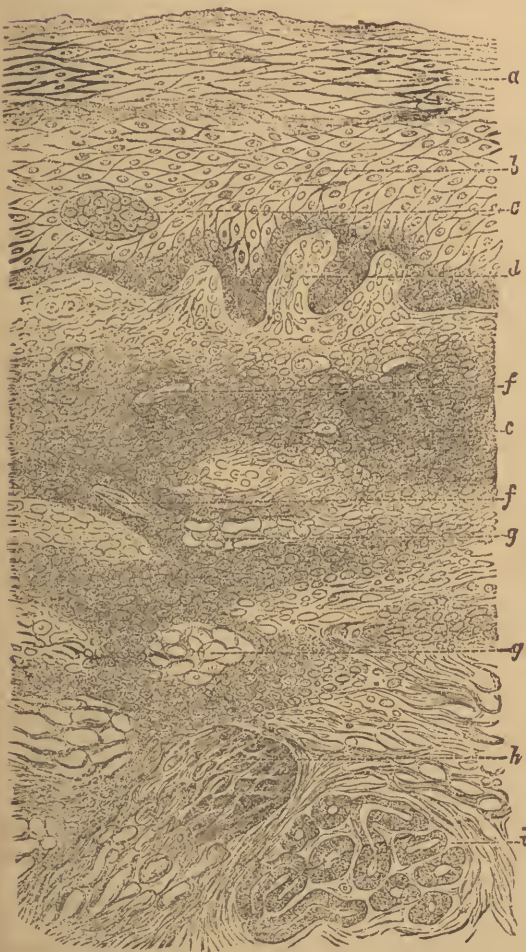
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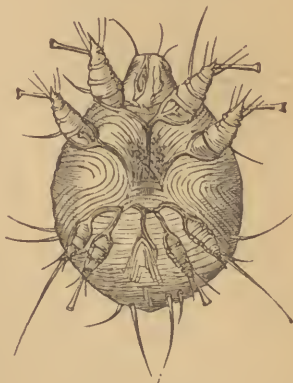
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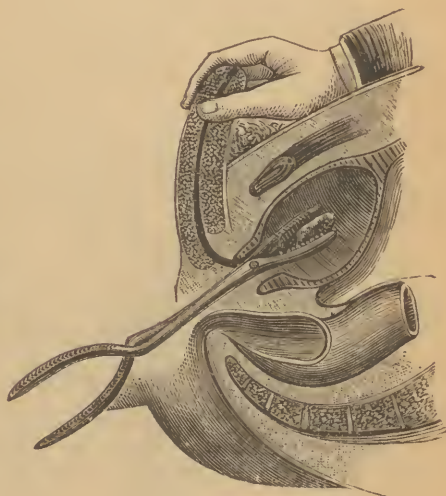
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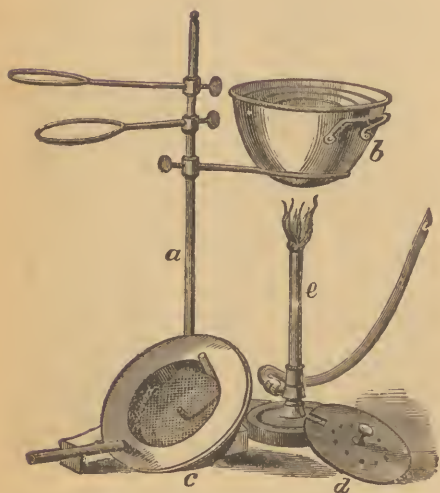
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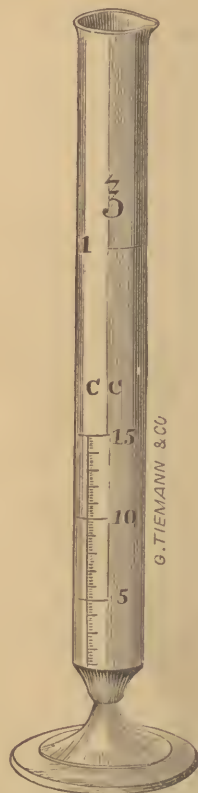
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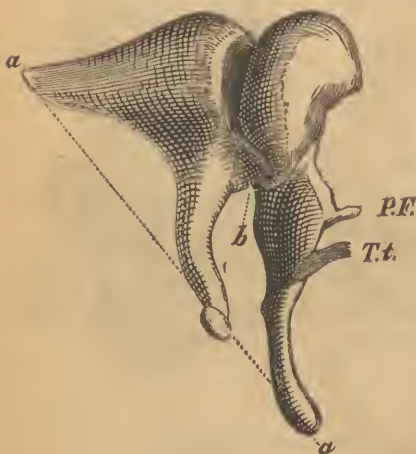
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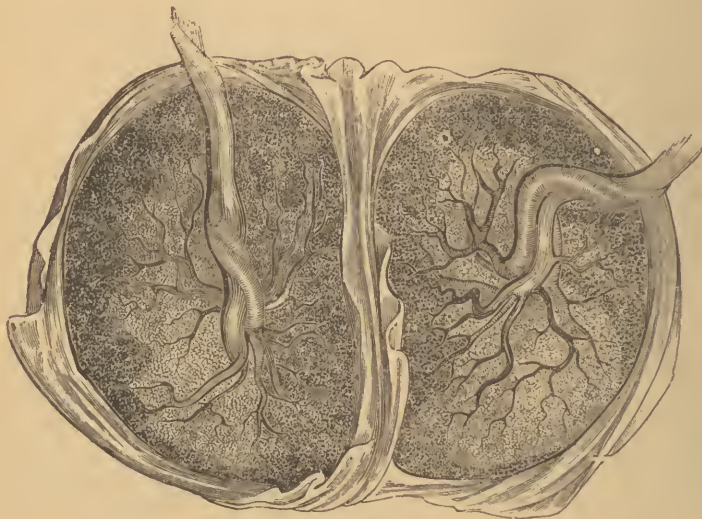
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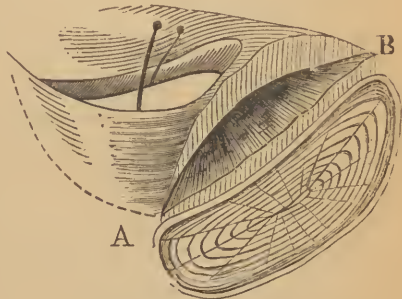
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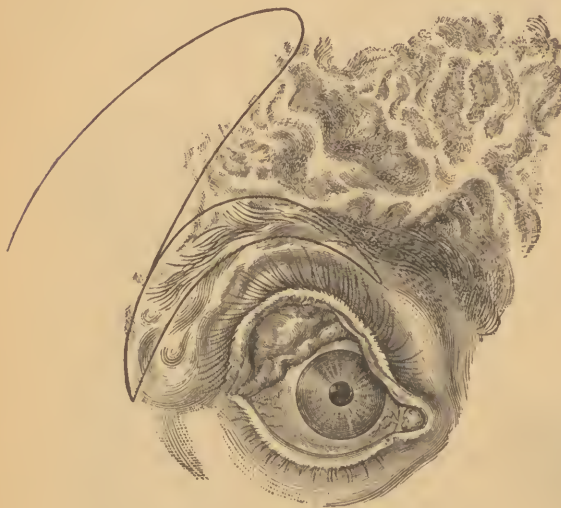
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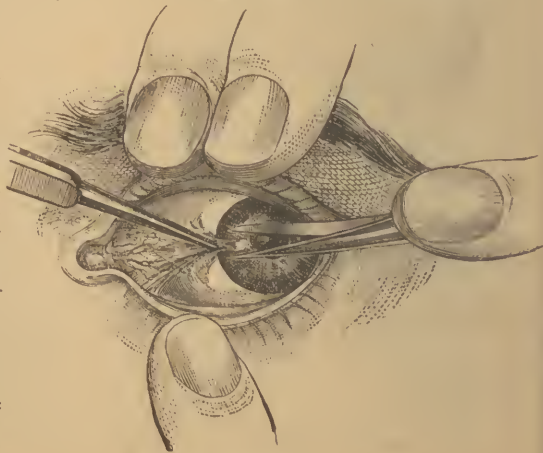
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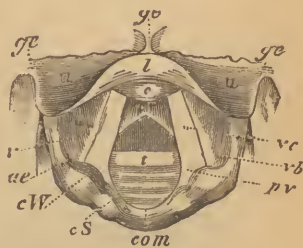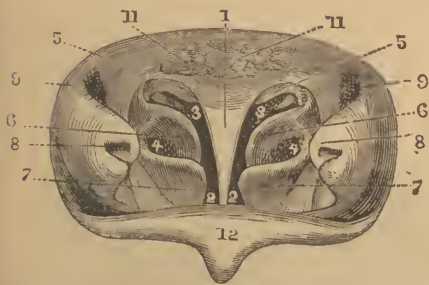
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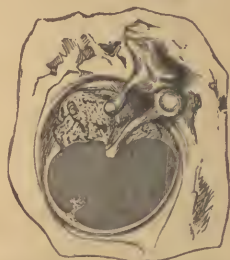
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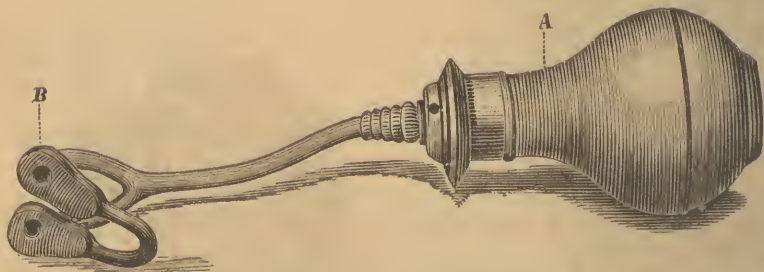
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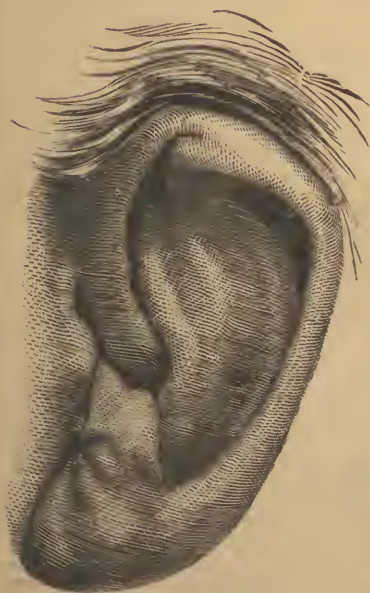
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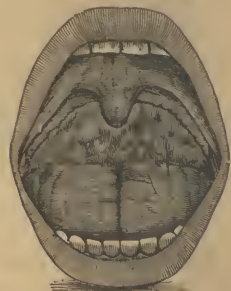
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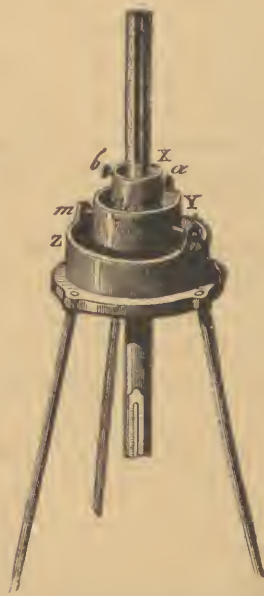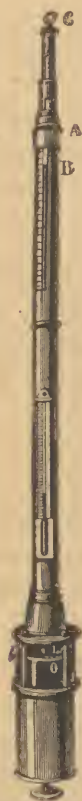
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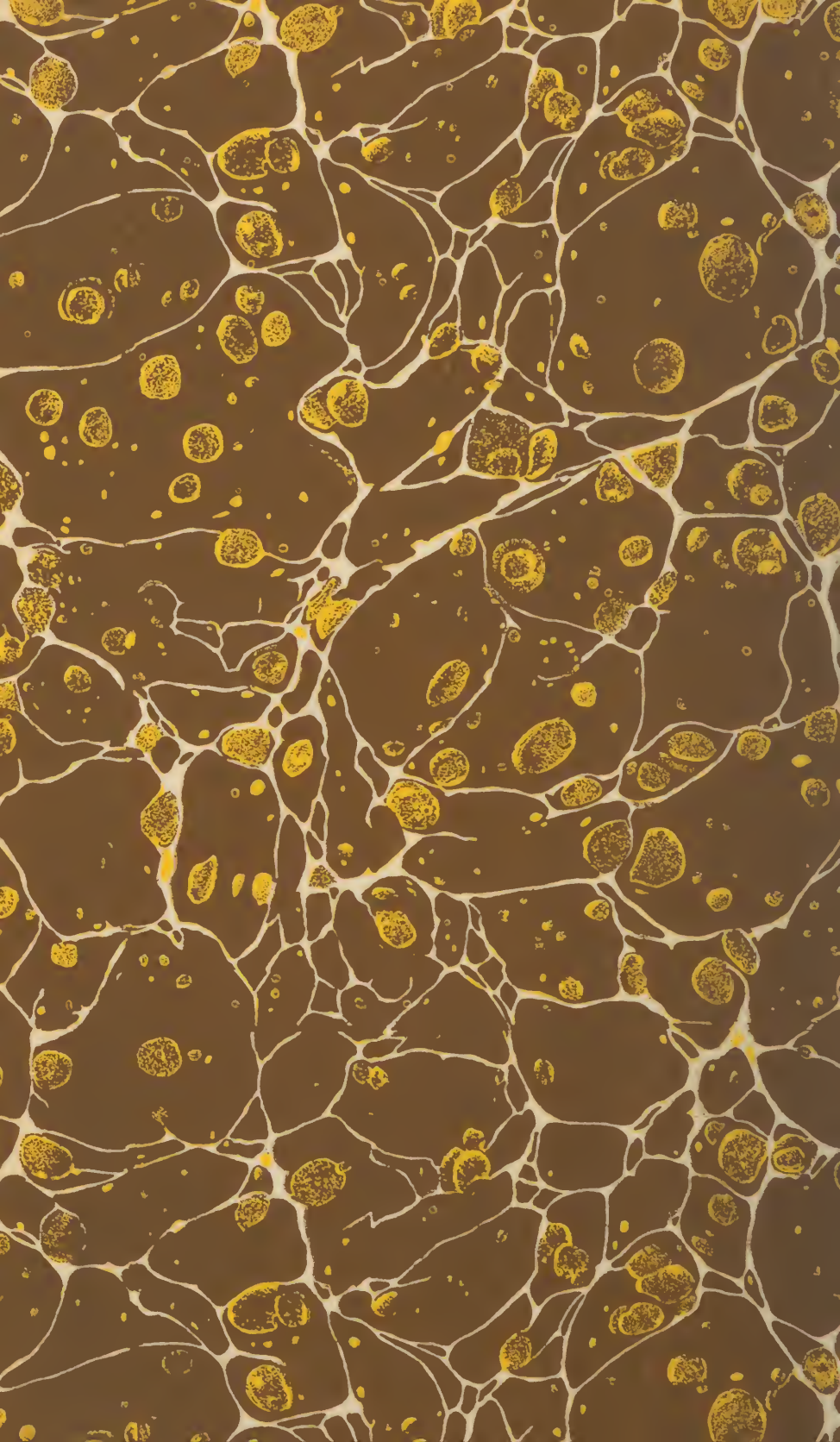
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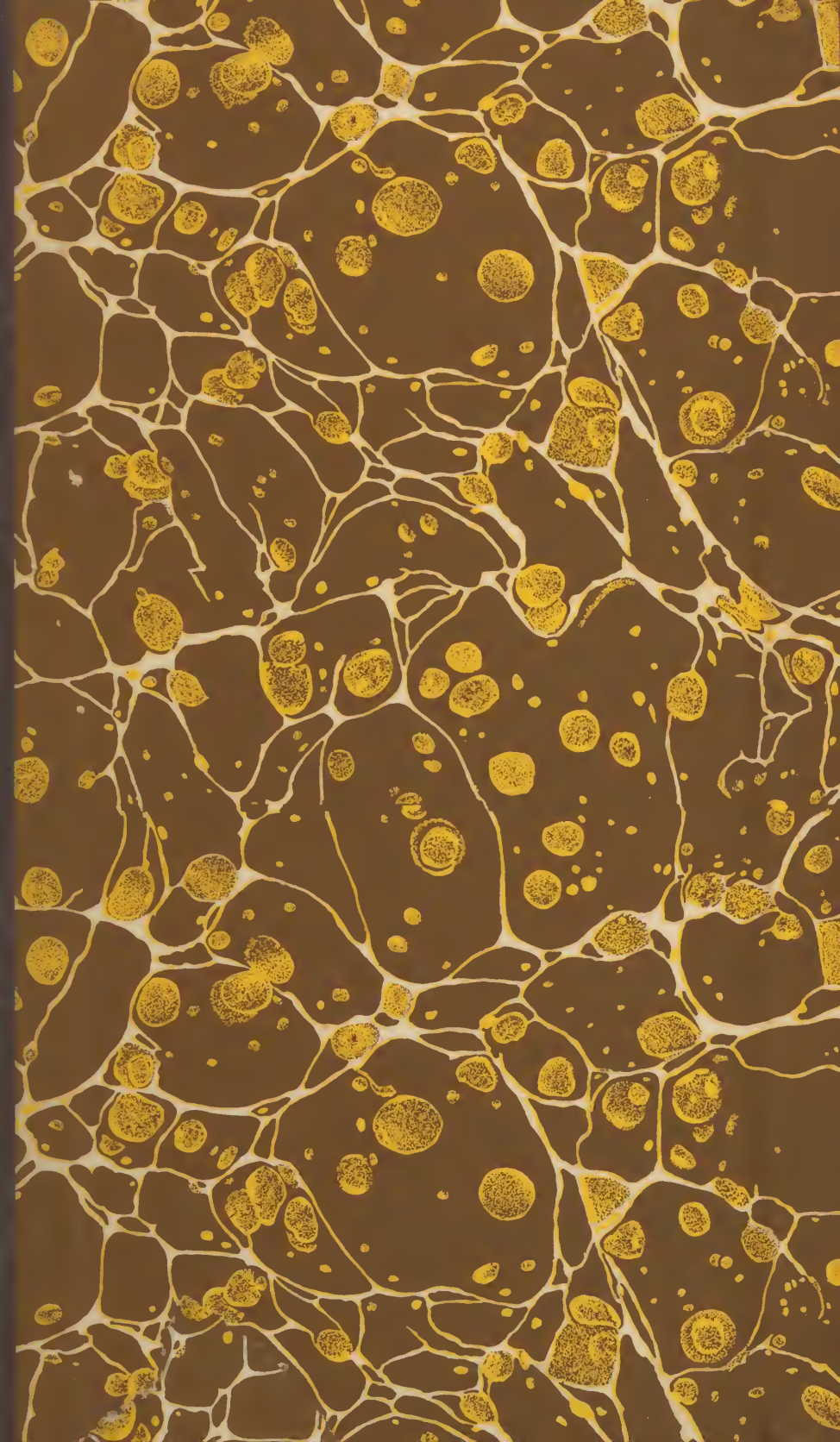
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